

# RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

Vol. 57

DECEMBER, 1951

No. 6

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# RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

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## "Single-Portal-Massive-Dose" X-Ray Therapy Technic for Certain Upper Respiratory Tract, Parotid Gland, and Recurrent Breast Cancers<sup>1</sup>

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New York, N. Y.

THE THESIS OF this presentation is that the skin of certain regions can tolerate a radiation dose as large as 8,000 r to a single portal, in four to five weeks, and that certain tumors with metastatic nodes, unsatisfactorily irradiated with other current technics, can be brought into the range of radiocurability by the use of this dosage.

The two-portal cross-firing technic originally described by Coutard delivered a relatively large tissue dose to the mid-plane of the neck. When the tumor was situated in the midline, the effect was satisfactory despite the intense epithelitis. When, however, the tumor was unilaterally placed (for example, a flat infiltrating carcinoma of the tonsil with a metastatic carotid node), the normal tissues received an unduly heavy dose, whereas the tonsillar carcinoma and node were inadequately irradiated.

Let us examine a hypothetical carcinoma of the tonsil situated 4 cm. below the skin, with a unilateral node at a depth of 2 cm. With the original Coutard technic of two cross-firing portals, the skin dose would be 4,000 r to each field, the dose to the tonsil 4,300 r, and to the node 4,500. Both the primary tumor and the node would receive

a relatively small amount of radiation, lethal to only a small group of radiosensitive carcinomas. Furthermore, the patient would suffer the serious discomfort of a marked epithelitis, which often prevents the administration of the contemplated total dose. If it were possible to deliver the total skin dose of 8,000 r to a single portal, the dose to the tonsil would be 5,400 r, and to the more radioresistant node 7,000 r. By this means, a much larger tumor dose would be received.

The question which immediately arises is whether the skin can tolerate these larger doses.

Earlier studies (1, 2) demonstrated that many skins are radio-immune, and can tolerate doses much larger than 4,000 r to an 8 × 10-cm. field in twenty-eight days. The following was the type of experience which led to the single-portal-massive-dose technic to be described here.

### CASE REPORT

H. E. had an extensive carcinoma of the mucosa overlying the medial surface of the jaw and extending back onto the tonsillar pillar and lower portion of the buccal mucosa. The tumor measured 4 × 6 cm. Its medial surface was 3 cm. from the surface of the skin, except for the posterior margin, which

<sup>1</sup> From New York University Hospital and Hospital for Joint Diseases, New York, N. Y. Presented at the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 10-15, 1950.

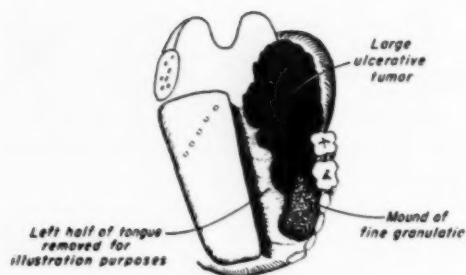


Fig. 1. Case H. E.: Squamous-cell carcinoma of medial surface of jaw extending back to the buccal mucosa and tonsil. There were two metastatic nodes in the submaxillary triangle.

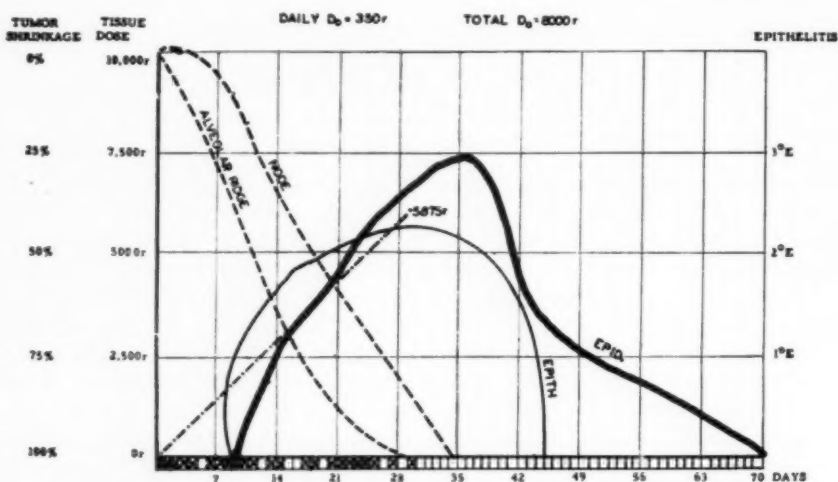


Fig. 2. Case H. E.: Graphic record of treatment, reactions, and tumor shrinkage.  $D_0 = 8,000$  r in thirty days. Dose to primary tumor 5,875 r; to submaxillary nodes 7,440 r. There was complete disappearance of the tumor at conclusion of treatment. Epidermitis reached a third-degree intensity on the thirty-sixth day and healed on the seventieth day.

was 4.5 cm. from the skin (Fig. 1). There were two metastatic nodes in the submaxillary triangle. Microscopically the tumor was a moderately undifferentiated squamous-cell carcinoma (Fig. 3). Radiation (h.v.l. 1.0 mm. Cu) was delivered through a single portal,  $8 \times 10$  cm., encompassing the primary tumor and metastatic nodes. The skin dose ( $D_0$ ) was 350 r daily, totaling 8,000 r in thirty days. The chronologic treatment events are illustrated in Figure 2.

On the eleventh day the dose ( $D_0$ ) to the primary tumor reached 2,100 r. Clinical shrinkage was 50 per cent. Serial biopsy showed moderate acute cell death and radiation keratogenesis (Fig. 4). It was estimated that there was approximately 35 per cent destruction of the tumor cells. The skin erythema had not yet reached a first-degree intensity, although the skin dose by this time amounted to 3,150 r. From the biopsy it was concluded that

the histologic destruction was unsatisfactory and that the relatively radio-immune skin could tolerate further irradiation.

By the twenty-fifth day, the skin dose was 6,600 r, and the dose to the primary tumor 5,200 r. Clinically the latter had shrunk 90 per cent. Histologically (Fig. 5) there was approximately 75 per cent destruction of tumor cells. The skin erythema had reached a second-degree intensity. The epidermitis, also of second-degree intensity, was confined to the left side of the mouth, producing slight discomfort. It was concluded from the biopsy that the irradiation effect was still unsatisfactory, and that, despite the epidermitis from a skin dose of 6,600 r, additional treatment was necessary. Irradiation was continued to a total

skin dose of 8,000 r in thirty days. This delivered 5,875 r to the primary tumor and 7,440 r to the nodes.

On the thirty-fifth day the skin reaction (Fig. 6) had reached its maximum intensity. This was slightly less than a third-degree epidermitis, as evidenced by the fact that the denudation did not extend to the outer border of the irradiation field and that some of the subsequent healing occurred from epithelial islands near the center of the field. The primary tumor and nodes had disappeared clinically.

On the forty-second day the epidermitis was healing rapidly (Fig. 7) despite the large skin dose. This confirmed the earlier deduction of a radio-immune skin. Healing was complete on the seventieth day.

Five months after institution of treatment there were only slight atrophy and depigmentation of skin

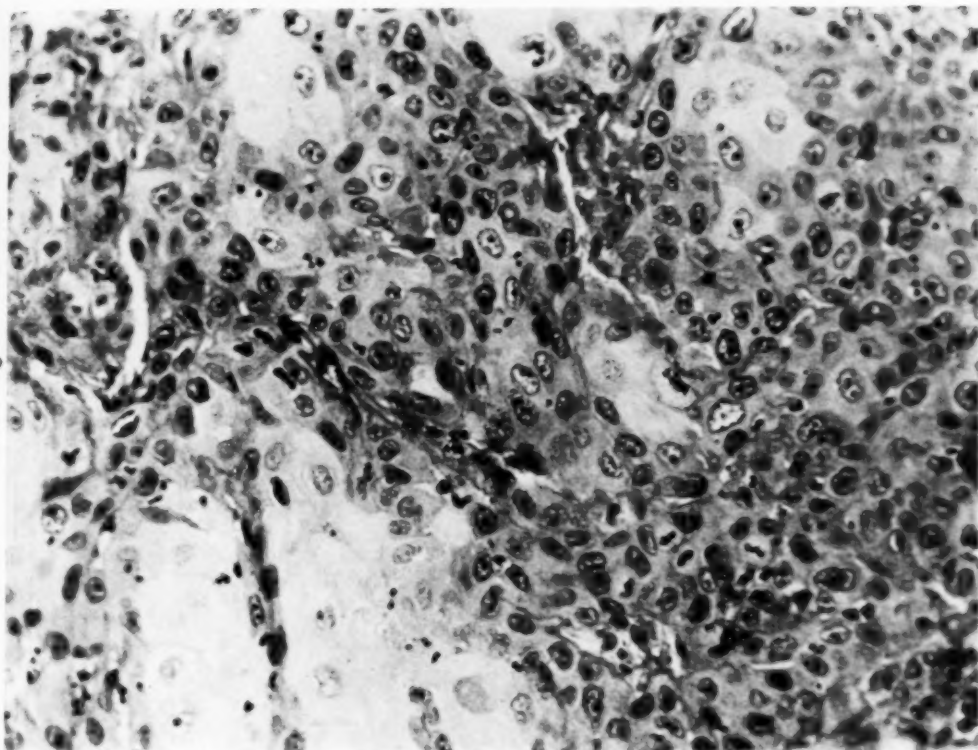


Fig. 3. Case H. E.: Biopsy before treatment: moderately undifferentiated squamous-cell carcinoma.

(Fig. 8). The epidermitis curve, shown in Figure 2, closely paralleled the average epidermitis curve of 21 patients who received skin doses ranging from 7,000 to 8,000 r (Fig. 11).

One year later, there was a recurrence of the primary tumor at its posterior margin overlying the tonsil. In this region the greater depth of the tumor from the skin (4.5 cm. as compared with 3 cm. for the major portion of the tumor) and its location at the periphery of the beam (where the tissue dose is lower) reduced the tumor dose to approximately 5,000 r. The patient eventually died of the recurrence. This observation provided an accurate estimation of the tumor lethal dose; *i.e.*, 5,875 r in thirty days was lethal, whereas 5,000 r in the same time was sublethal. Observations of this type served to substantiate the accuracy of many of the points in the scatter diagram of Figure 28.

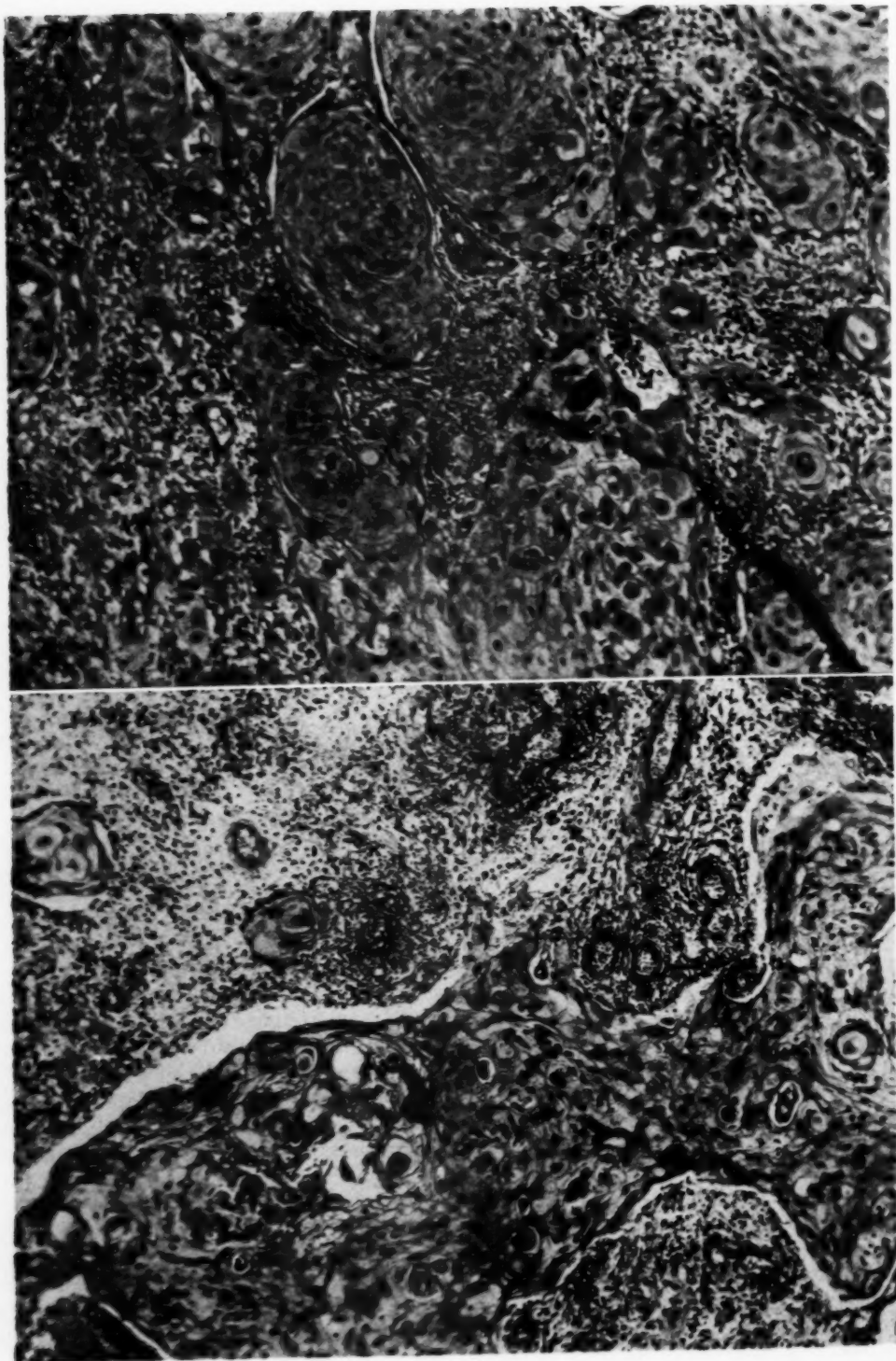
*To summarize:* This case illustrates: a typical average skin reaction following a skin dose of 8,000 r in thirty days; the role of serial biopsies in clinical radiation therapy; one criterion for the employment of the single-portal-massive-dose technic;

and the effectiveness of this technic against metastatic squamous-cell carcinoma in cervical nodes moderately radioresistant.

#### TECHNIC AND MATERIAL

Earlier investigations (1) of skin reactions showed that the skin and mucosa of one-fourth of all adult patients were relatively radio-immune and could tolerate large doses of roentgen radiation. About ten years ago, we began progressively to increase the total dose delivered to one skin portal on the head and neck from 4,000 to 6,000 r, and finally to 8,000 r.

The technic of irradiation was simple. Radiation qualities ranged from 1.0 to 2.0 mm. Cu h.v.l., except for four patients who were treated with radiation of 10 mm. Cu h.v.l. (1,000 kv.). Only one portal was used. Field size was  $8 \times 10$  cm. in more than 95 per cent of the cases. In a few instances this was increased to  $10 \times 10$  cm.



Figures 4 and 5  
(See opposite page for legend)





Fig. 6. Case H. E.: Thirty-fifth day. Maximum epidermitis approaching third-degree intensity.

Fig. 7. Forty-second day. Beginning healing of epidermitis.

Fig. 8. Five months after first treatment. Slight atrophy and depigmentation of skin.

or  $8 \times 12$  cm. in order to include all metastatic nodes.

The daily skin dose ranged from 300 to 400 r, the optimum being 325 r. This was designed to deliver an average daily tumor dose of 225 to 275 r. The term, average daily tumor dose, refers not to the dose from each treatment but the average obtained by dividing the total tumor dose by the total over-all treatment time in days. Previous studies (3) have indicated that the optimum average daily tumor dose for squamous-cell carcinoma treated with external irradiation is from 225 to 275 r.

It was most convenient to plan the fractionation on the basis of a weekly dose of 1,600 to 1,900 r, depending upon whether five or six treatments a week were given. The optimum total skin dose to one portal was 7,000 to 8,000 r, delivered over a period of four to five weeks. The distribution of cases in this series receiving varying total skin doses was as follows:

Range in r	Number
4,001-5,000.....	6
5,001-6,000.....	21
6,001-7,000.....	19
7,001-8,000.....	21
8,001-8,450.....	7

Although it is recommended that the "over-all time" for the duration of treatments be twenty-nine to thirty-five days,

nevertheless, in this series many cases were treated otherwise. The distribution of the "over-all treatment time" was:

Range in Days	Number of Cases
15-18.....	4
19-22.....	12
23-26.....	14
27-30.....	17
31-34.....	10
35-38.....	5
39-42.....	5
43-46.....	2
47-50.....	2
51-54.....	2
55-58.....	1

#### INDICATIONS FOR SINGLE-PORTAL TECHNIC BASED ON DEPTH OF TUMOR FROM SKIN

The single-portal technic is indicated for lesions whose deepest extension is not more than 4 cm. from the skin. With an  $8 \times 10$ -cm. field and a total skin dose of 8,000 r, the tumor dose at 4 cm. depth is 5,360 r. If a hypersensitive skin prevents administration of a total skin dose of 8,000 r, the tumor dose at 4 cm. depth might be sublethal in many cases. In 7 patients in this series, the remotest portion of the tumor was more than 4 cm. from the skin, and in every instance there was residuum or recurrence. H. E., cited above, was one of this number. The factor of "depth of tumor from skin" is the paramount indication for this technic.

Fig. 4. Case H. E.: Biopsy on eleventh day when tumor dose had reached 2,100 r. Moderate acute cell death and radiation keratogenesis, and slight vacuolation. Grossly the tumor had shrunk 50 per cent.

Fig. 5. Case H. E.: Biopsy on twenty-fifth day when tumor dose had reached 5,200 r. Approximately 75 per cent of the tumor cells have disappeared, bringing the tumor stroma into view. The remaining tumor cells show marked radiation keratogenesis and slight vacuolation. Grossly the tumor had shrunk 90 per cent.



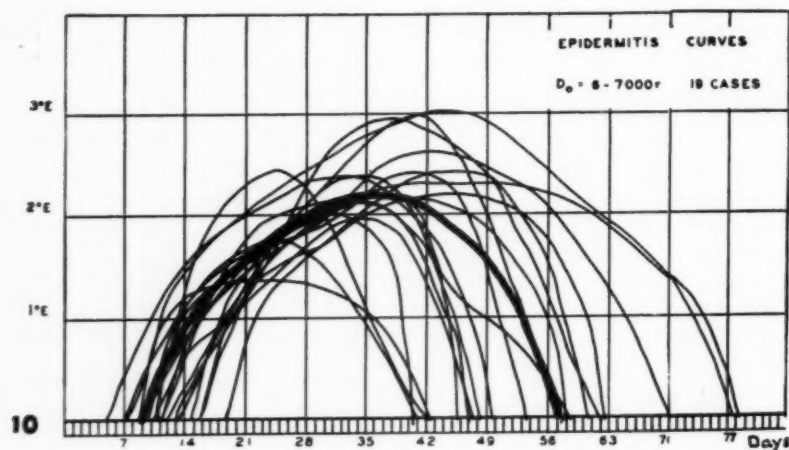
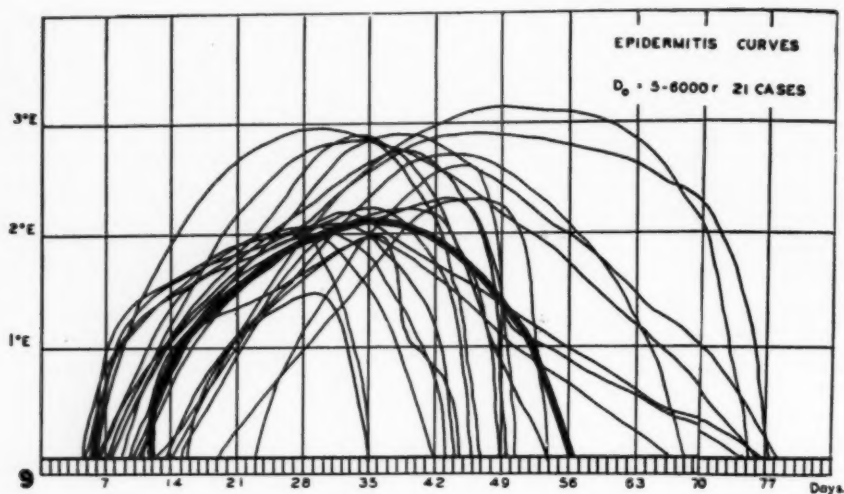


Fig. 9. Epidermitis curves of 21 patients receiving skin doses of 5,000 to 6,000 r. The heavy line is the average curve, mathematically derived.

Fig. 10. Epidermitis curves of 19 patients receiving skin doses of 6,000 to 7,000 r. The heavy line represents the average curve, mathematically derived.

In this series of cases, the distribution of skin-tumor distances (to the deepest portion of the tumor) was as follows:

Skin-Tumor Distance (cm.)	Number of Cases
2.5.....	3
3.0.....	15
3.5.....	12
4.0.....	30
4.5.....	6
5.0.....	5
5.5.....	3

The technic is recommended for:

1. Flat carcinoma of the tonsil which infiltrates the pterygoid fossa, with or without metastatic nodes.
2. Carcinoma of the retromolar fossa, moderately advanced or advanced, especially if too extensive for intra-oral irradiation.
3. Extensive carcinoma of the tonsillar pillar which does not approach the midline.
4. Carcinoma of the lateral wall of the oropharynx and hypopharynx.

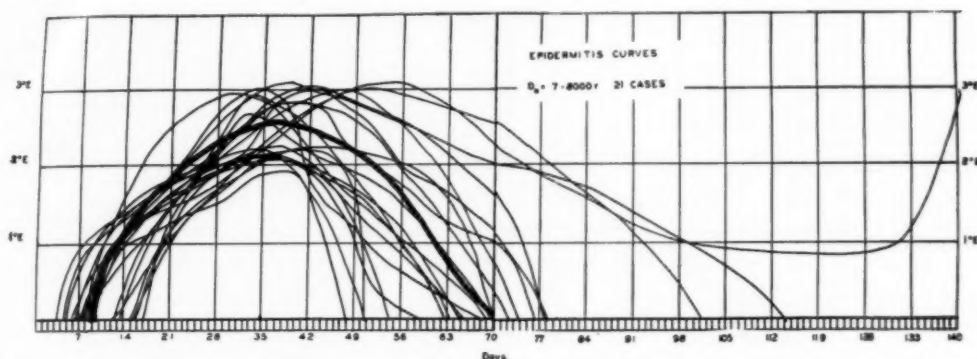


Fig. 11. Epidermitis curves of 21 patients receiving skin doses of 7,000 to 8,000 r. The heavy line represents the average curve, mathematically derived. One skin reaction failed to heal and resulted in necrosis.

5. Carcinoma of the dorsum of the base of the tongue whose deepest portion does not extend more than 4 cm. from the skin.
6. Carcinoma of the pyriform sinus.
7. Carcinoma of the aryepiglottic fold, less than 4 cm. from the skin.
8. Extensive carcinoma of the larynx, unilateral. (This technic has been useful in several cases of advanced carcinoma with nodes. See Figs. 17-19.)
9. Carcinoma of the lateral floor of the mouth, moderately advanced, with metastatic nodes.
10. Unilateral metastatic carcinoma in cervical nodes of undetermined origin. In lesions of this type, the primary tumor is frequently unwittingly incorporated within an 8 × 10-cm. field. (See Figs. 20-22.)
11. Isolated metastatic cervical nodes, primary tumor arrested with previous treatment.
12. Carcinoma of the parotid gland (squamous-cell carcinoma or adenocarcinoma) with or without metastatic nodes. Certain radioresistant desmoplastic cylindromatous carcinomas excluded from this category.
13. Recurrent carcinoma of the breast; bulky tumors on the anterior chest wall of subcutaneous or internal mammary node origin.

The single-portal-massive-dose technic

can occasionally be employed for tumors which extend to the midline, with the addition of supplementary irradiation to that portion of the tumor more than 4 cm. from the skin. For carcinoma of the faucial arch, supplementary treatment can be provided by intra-oral irradiation; for carcinoma of the hypopharynx or extrinsic larynx, by means of a narrow beam of x-rays through the anterior or opposite lateral neck; for certain carcinomas of the posterior portion of the tongue, by interstitial irradiation.

#### SKIN AND MUCOSAL REACTIONS

Skin reactions were studied by constructing composite graphs of epidermitis curves produced by successive dose levels from 4,000 to 8,500 r in ranges of 1,000 r (Figs. 9-13). An average epidermitis reaction curve (heavy line) was obtained for each range. In a previous publication (1), curves based on two portals cross-firing the lower head and neck were illustrated. Like these, the present curves show a greater uniformity during the destructive phase (first twenty-eight days), when skin reactions are ascending, than during the subsequent healing phase. This is due to the greater individual variation during recovery.

It is important to ascertain early in the course of treatment, during the destructive phase, whether a particular skin is radio-immune or radiosensitive. In the latter event, it may be impossible to deliver a

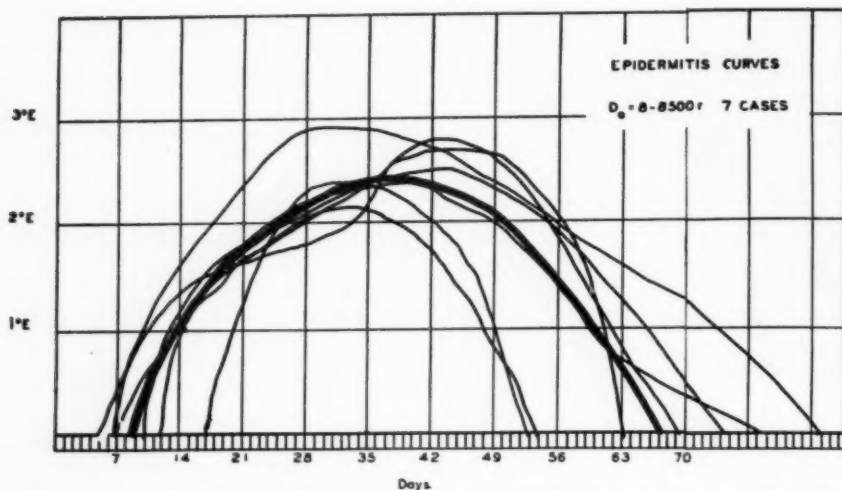


Fig. 12. Epidermitis curves of 7 patients receiving skin doses of 8,000 to 8,500 r. The heavy line represents the average curve, mathematically derived.

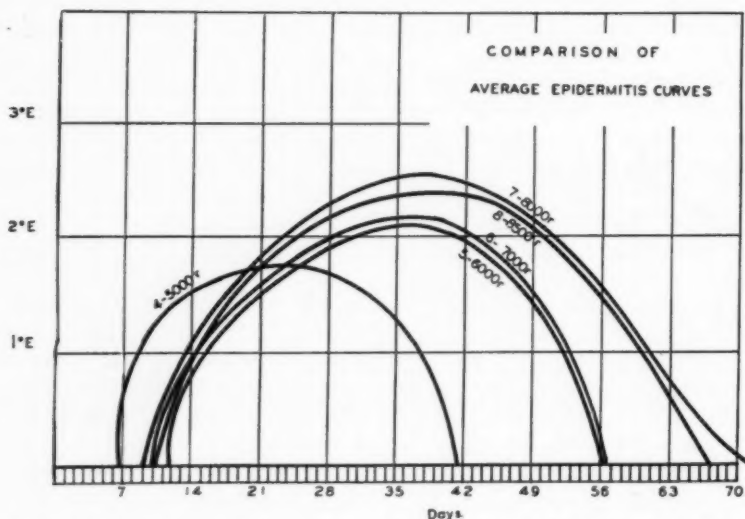


Fig. 13. Average epidermitis curves taken from Figures 9-12. Note the significant difference in intensity of reaction between skin doses above and below 7,000 r.

desired total skin dose of 8,000 r. When the skin is radiosensitive, the reaction starts early and ascends rapidly. When the skin is radio-immune, the reaction starts later and ascends at a slower rate, while healing occurs earlier. The graphs in Figures 9-12 serve as a useful reference when one is attempting to decide in a given case how much radiation the skin can tolerate. Comparison of a particular skin

reaction with these graphs on the seventh, fourteenth, and twenty-first days, when the skin dose is approximately 1,500, 3,000, and 4,500 r respectively, may aid the radio-therapist in determining the maximum skin tolerance dose. It is desirable to plot reaction curves for each case during the progress of the treatment, as illustrated in Figures 2 and 18.

The intensity and duration of the skin



Fig. 14. Mild radiation sequela of skin four months after a skin dose of 6,000 r in twenty-four days.

illustrates the maximum skin reaction on the forty-sixth day in a patient who received 7,000 r ( $D_0$ ) in thirty-five days, while Figure 16 shows the typical changes occurring one year later in the same patient.

The group of 21 patients who received skin doses ranging from 7,000 to 8,000 r in approximately twenty-eight to thirty-five days (Fig. 11) was the most significant one, because of the occasional severe reaction. The late skin changes ranged from mild atrophy with telangiectasis to necrosis. An example of a mild reaction is seen in Figures 17-19. These illustrate a case of carcinoma of the epiglottis with metastatic

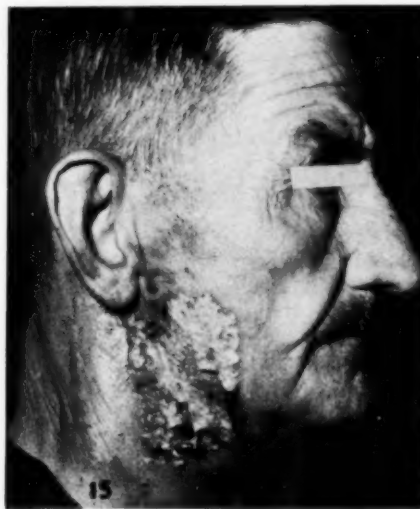


Fig. 15. Maximum skin reaction on forty-sixth day after a skin dose of 7,000 r in thirty-five days.



Fig. 16. Moderate radiation sequela of skin one year after a skin dose of 7,000 r in thirty-five days.

reaction are related to the total dose. Figure 14 shows the skin of a patient who, four months previously, had received 6,000 r ( $D_0$ ) in twenty-four days for a carcinoma of the tonsil and tongue. The late radiation changes, as is usual, were mild and remained so for four years.

With total skin doses of 7,000 r in thirty-five days the epidermitis healed within seventy-seven days in all cases, but late fibrosis and atrophy were more intense than in the previous group. Figure 15

cervical nodes (Fig. 17) irradiated with a skin dose of 7,800 r in thirty-five days through an  $8 \times 10$ -cm. field. Figure 18 is a graphic record of the treatment and response of the skin, mucosa, and tumor. Two years later the skin exhibited milder sequelae than usual (Fig. 19). An example of severe late fibrosis following a skin dose of 8,000 r in twenty-seven days is illustrated in Figures 20-22. The patient had a large cervical node containing metastatic squamous-cell carcinoma of undeter-



Fig. 17. Diagram of advanced carcinoma of the extrinsic larynx with metastases to cervical nodes.

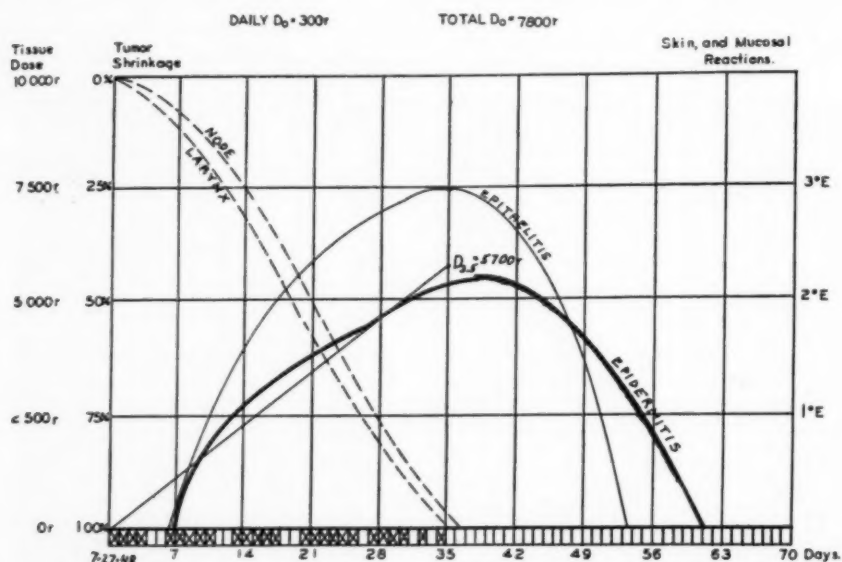


Fig. 18. Graphic record of treatment reactions, and tumor shrinkage of carcinoma of extrinsic larynx illustrated in Figure 17. The skin dose was 7,800 r in thirty-five days. No recurrence since treatment in July 1948.

mined origin (Fig. 20). Treatment was given through a  $10 \times 10$ -cm. field with the hope that the primary tumor would lie within the beam of radiation. The third-degree epidermitis healed three and one-half months after the first treatments (Fig. 21), resulting in marked atrophy, depigmentation, and fibrosis. The fibrosis became more intense, but ulceration did not occur. Five years later (Fig. 22) the patient was free of disease.

Figure 11, showing the epidermitis curves for skin doses of 7,000 to 8,000 r, includes three severe reactions. Two of these

finally healed. The other never healed completely and soon progressed to massive necrosis (Fig. 23). Paradoxically, this outcome could not have been anticipated, since the early epidermitis curve is seen to ascend later than the average, reaching second-degree intensity on the thirty-first day, as compared with the twenty-third day for the average. A possible explanation is that the observed reaction is a function of the epidermis, whereas eventual healing or necrosis is a function of the subcutaneous connective tissues and blood vessels. If connective-tissue damage is



mild and the vascularity is not unduly impaired, the epidermis will heal. The three severe reactions included in Figure 11 were produced by 7,600 r in twenty-two days, 7,900 r in twenty-five days, and 8,000 r in twenty-seven days. Evidently, the over-all time was too short for these large skin doses. It was concluded that if the skin dose is greater than 7,000 r, it should be spread over a period of at least thirty-five days.

Most of the milder reactions from skin doses of 7,000 to 8,000 r occurred when the over-all time was approximately thirty-five days or longer. Figure 24, for example, shows a patient with a massive carcinoma of the retromolar fossa, buccal mucosa, and faucial arch. Two months following a skin dose of 8,000 r delivered in fifty-two days, a small residuum of radioresistant tumor was excised. The incision through the irradiated skin healed by primary union.

One of the 4 patients successfully treated with one-million-volt radiation had a flat, infiltrating, ulcerating carcinoma of the tonsil with extension into the pterygoid fossa and metastasis to a carotid node. Figure 25 shows the maximum skin reaction (epidermitis sicca) one week after a skin dose of 7,800 r in thirty-five days. As is customary with supervoltage radiation, the immediate skin reaction is milder than that produced at 200 kv. Four months later (Fig. 26) there was mild depigmentation in the central portion of the irradiated skin with no fibrosis or thickening. One year later, there was progression of the subcutaneous fibrosis, forming a dense, board-like plaque. Finally, three years after treatment, a large radionecrotic ulcer resulted, requiring two years to heal. The patient is free of disease six years after onset of treatment (Fig. 27).

Aside from the one case following irradiation at 200 kv. (Fig. 23), there was no other instance of necrosis. With this ray quality, the subcutaneous fibrous plaque, when it occurs, is seldom more than 1 cm. thick and can be sustained by the adjacent tissues (Fig. 22). When supervoltage therapy is employed, the more effective penetration

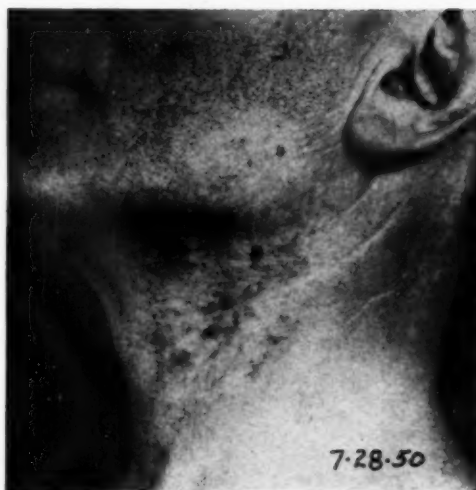


Fig. 19. Moderate radiation sequelae two years after 7,800 r in thirty-five days in case shown in Figure 17.

tends to produce, after several years, a thicker plaque of avascular fibrous tissue. This may more readily succumb to ischemic necrosis (Fig. 27). There is a difference, therefore, in the late skin reactions between 200 kv. and 1,000 kv. With 200 kv. a skin dose of 8,000 r may be given and will produce sequelae in the superficial layers of the skin. With 1,000 kv. it is dangerous to exceed a skin dose of 6,000 r, as the deep fibrosis may initiate sequelae in the deeper tissues which secondarily affect the epidermis.

Only 7 patients received skin doses greater than 8,000 r (Fig. 12). No severe skin reactions occurred in this group. The sample is too small, however, to be significant. As is demonstrated by the graph, some skins can tolerate very large doses. It is interesting to note that two of the patients received 8,100 r in twenty-eight and twenty-nine days respectively. One patient received 8,900 r in thirty-five days and his reaction healed. He was not included in this group because the field size was small ( $5 \times 5$  cm.). It will be useful to procure standard reaction curves for fields of this small area.

In Figure 13, the average epidermitis curves from Figures 9-12 are compared.

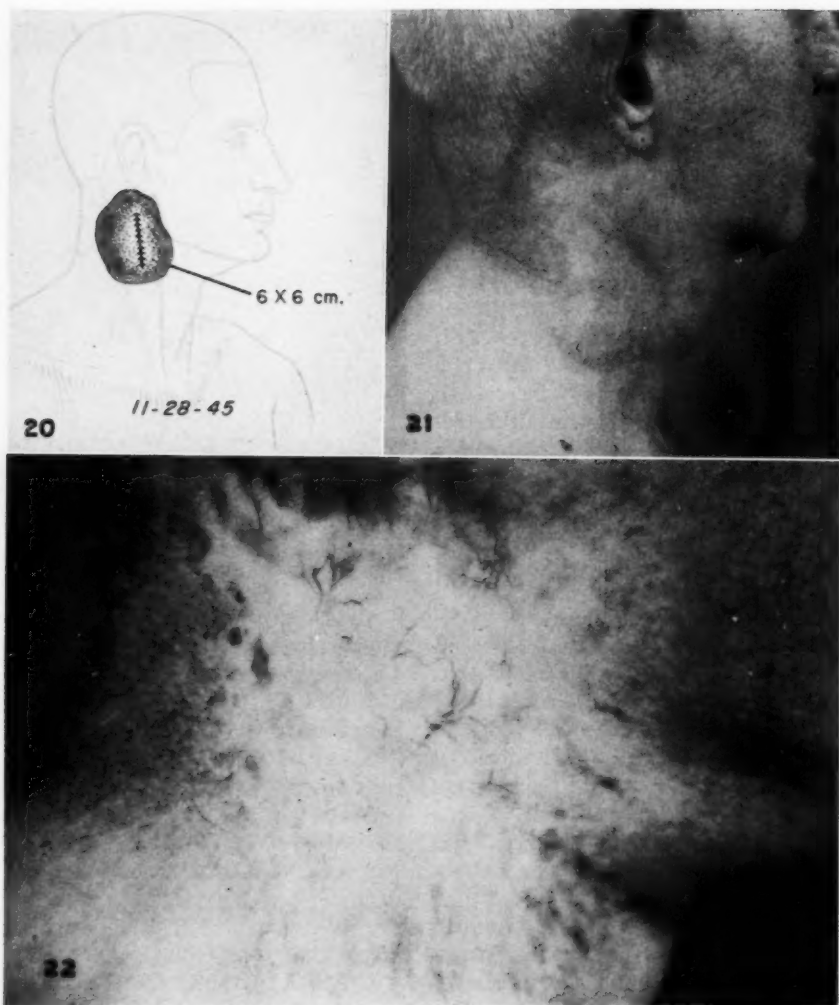


Fig. 20. Metastatic squamous-cell carcinoma. Primary site undetermined.

Fig. 21. Marked atrophy and fibrosis three and a half months after a skin dose of 8,000 r in twenty-seven days.

Fig. 22. Severe cutaneous and subcutaneous fibrosis five years after 8,000 r in twenty-seven days. No ulceration. No evidence of recurrence five years later.

In addition, there is an average curve for doses of 4,000 to 5,000 r. This latter group contained only 6 cases, a small sample yielding a somewhat distorted average curve. The striking feature of the average curves, as shown in the figure, is the similarity of the pairs of curves above and below 7,000 r. Study of the reaction curves suggests that, with the single-portal-massive-dose technic, the danger of severe reaction

or necrosis lies with the occasional atypically radiosensitive skin.

Late skin effects have not been thoroughly evaluated, as only 22 cases have been followed for more than two years. With skin doses below 6,000 r in twenty-eight days, there are moderate fibrosis and thickening of the subcutaneous tissues, producing little or no discomfort. With skin doses from 7,000 to 8,000 r it is com-

mon for the skin to show slight fibrosis and atrophy shortly after the primary reaction heals. In a majority of instances, however, there occur, after one or two years, marked atrophy, devascularization, and board-like thickening of the skin and subcutaneous tissues, ranging from 0.5 to 1.0 cm. in thickness. A plane of demarcation appears between relatively healthy tissue and the board-like plaque. Late roentgen



Fig. 23. Appearance of skin two months after a skin dose of 7,600 r in twenty-two days. Primary radionecrosis of skin. The reaction never healed. This was the only instance of radionecrosis in 70 patients irradiated with 200-kv. x-rays. The primary tumor was an advanced carcinoma of the tongue. There was subsequent necrosis of part of the right mandible. The overall treatment time of twenty-two days was too short for this large dose. (Compare with Figure 24.)

keratosis and carcinoma, though possible, have not yet been observed in this series. The possibility of these sequelae is of little consequence in the treatment of moderately advanced or advanced cancer.

Mucous membrane reactions (epithelitis) were very mild and only rarely debilitating, compared with the reactions with the cross-firing Coutard technic. These reactions were too irregular for satisfactory statistical or graphic analysis. The majority were of first-degree intensity. The mildness of the symptoms from epithelitis is due to its unilaterality and is an important advantage of the single portal technic.



Fig. 24. Healed scar of operation performed three months after a skin dose of 8,000 r in fifty-two days. Skin doses larger than 7,000 r should be administered over a period of thirty-five days or longer to preserve the vitality of the tissues. Compare Figure 23.

#### TUMOR LETHAL DOSE FOR EPIDERMOID CARCINOMA OF UPPER RESPIRATORY TRACT

The single-portal-massive-dose technic afforded a useful opportunity for studying tumor lethal dose because of the uncomplicated pattern of distribution of radiation throughout the tumor. Figure 28 is an "over-all time-dose" scatter diagram of the lethal doses for 26 primary epidermoid carcinomas of the mouth, pharynx, and larynx, and 25 metastatic cervical nodes. Each circle represents the tumor lethal dose given over a specified number of days to a primary tumor, while the dots represent metastatic nodes.

A number of these points represent not the actual dose given, but the corrected tumor lethal dose. The following examples illustrate how corrections were made. A carcinoma of the lateral margin of the tongue extended medially so that the deepest portion received a tumor dose of 6,000 r in thirty days. Two years later, a recurrence appeared only at the deep portion of the tumor. The tumor lethal dose was then corrected to 6,500 r in thirty days. If the recurrence had appeared two months after treatment, the tumor lethal dose would be corrected to 7,000 r in



Fig. 25. Maximum reaction produced by supervoltage radiation. Skin dose was 7,800 r in thirty-five days.



Fig. 26. Patient shown in Figure 25. Healed skin four months after 7,800 r in thirty-five days with 1,000-kv. x-rays. The reaction was deceptively mild.



Fig. 27. Healed radionecrotic ulcer in same patient six years after supervoltage irradiation. Ulceration commenced three years after treatment.

thirty days. There were corroboratory observations: in the above example, the lateral margin of the tongue originally received 7,000 r in thirty days, and no recurrence appeared. Another example is illustrated in Figure 1. Here the recurrence appeared at the periphery of the tumor, where the dose was 5,000 r, and not in the center of the tumor, where the dose was 5,875 r in thirty days. This afforded a rather exact estimate of the tumor lethal dose. Another type of correction was afforded when, at the conclusion of treatment, the tumor had disappeared clinically but a serial biopsy showed residual tumor. The dose was corrected upward.

Although these corrections were somewhat arbitrary, they utilized additional

information to achieve a more accurate estimate of tumor lethal dose. Sixteen of the 26 points for primary tumors (circles) were corrected upward. Only one point was corrected downward. This was done because the primary tumor as well as the node shrank very rapidly, and serial biopsies indicated complete tumor destruction early in the course of treatment when the tumor dose was still small.

Ten of the 25 points representing the nodes (dots) were corrected. In 5 instances, the node recurred; consequently, the tumor lethal dose was corrected upward. In 5 instances, the nodes shrank

unusually rapidly, or else the primary tumor was arrested by a considerably smaller dose, and consequently the tumor lethal dose was corrected downward.

The two oblique parameters in Figure 28 were drawn freehand for convenience in visual analysis of the diagram. They have no statistical significance. In the zone above the upper line are tumor lethal dose points for 10 cervical nodes. In the zone beneath the lower line are tumor lethal dose points for 7 primary tumors. In the middle zone is the time-dose range within which the tumor lethal dose is the same for primary tumors and metastatic nodes. From this chart it can be seen that the metastatic nodes are more radio-resistant than the primary tumors. This



is consistent with the opinion generally maintained, and contrary to Wood (4). From Figure 28, it can also be seen that the tumor lethal dose for primary epidermoid carcinoma of the mouth, pharynx, and larynx ranges from 4,200 to 6,300 r in approximately three to five weeks, whereas for metastatic nodes the range is from 5,000 to 7,500 r in three to five weeks.

finer. Radiation therapy of this lesion has been forsaken because of unsuccessful irradiation technic. Either the dose of external radiation has been inadequate or interstitial radium sources could not be properly distributed throughout the irregular regions occupied by the tumor. Parotid cancers are superficially located and seldom extend deeper than 4.0 cm. from

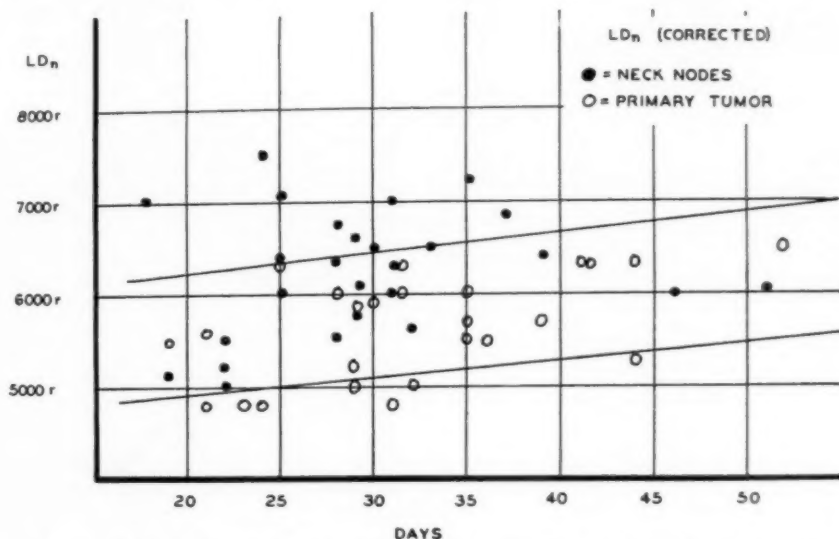


Fig. 28. "Over-all time-dose" scatter diagram of corrected lethal tumor doses for primary tumors and metastatic nodes of squamous-cell carcinoma of the head and neck. The parameters have been drawn freehand for convenient analysis of the data and have no statistical significance. Note that metastatic nodes require a larger lethal tumor dose than the primary tumors.

The single-portal-massive-dose technic satisfies the requirement for delivering a larger dose to the nodes than to the primary tumor.

Because of the small number of points on the scatter diagram, the mathematical construction of an average "over-all time-dose" regression curve is not warranted, as the statistical error is too great. However, a useful purpose is served by defining in a general way the tumor lethal dose range of a typical group of squamous-cell epitheliomas of the mouth, pharynx, and larynx, and their metastatic nodes.

#### CARCINOMA OF THE PAROTID GLAND

Lethal tumor doses for carcinoma of the parotid have never been satisfactorily de-

termined. Radiation therapy of this lesion has been forsaken because of unsuccessful irradiation technic. Either the dose of external radiation has been inadequate or interstitial radium sources could not be properly distributed throughout the irregular regions occupied by the tumor. Parotid cancers are superficially located and seldom extend deeper than 4.0 cm. from

the surface of the skin. Consequently, the single-portal-massive-dose technic is an ideal method of treatment, because the beam of radiation can reach the irregular ramifications of the tumor and deliver a proper tumor lethal dose. Six patients with carcinoma of the parotid were treated with this technic (Table I). Five are free of disease, 1 for five years, 2 for four years, 1 for two and a half years, and 1 for six months. Two of these successfully treated patients had metastatic nodes, which were included in the field of irradiation. The tumor lethal dose for these parotid carcinomas ranged from 4,380 r in twenty-three days to 6,786 r in thirty-six days. Five of these radiocurable lesions were cellular adenocarcinomas



TABLE I: PAROTID CANCER

Case and Date	Clinical Stage	Histological Type	Total D <sub>0</sub>	Minimal Tumor Lethal Dose	Over-all Treatment Time (Days)	Complications	Results
1. J. N. 2/19/47	Postoperative recurrence and one metastatic node (2 X 2.4 cm.) after 2 operations	Adenocarcinoma, low grade	8,000 r	6,720 r	28	Late necrosis of tragus which healed	Well four years
2. I. J. 8/25/45	Immediately postoperative after 2nd extensive resection which failed to remove the deep-seated tumor	Adenocarcinoma	6,900 r	4,761 r	35	Contractures of soft tissues of face	Well five years
3. A. F. 3/18/47	Postoperative recurrent tumor, 4 cm. diameter	Adenocarcinoma, Grade 3	7,900 r	4,380 r	23	None	Well four years
4. D. R. 7/23/48	In 1946 tumor removed and small amount of irradiation; in July 1948, large recurrent nodule partially removed	Adenocarcinoma, Grade 3	7,900 r	6,786 r	36	Slight fibrosis	Well two and one-half years
5. L. W. L. 9/1/50	Infiltrating tumor 4 X 5 cm. with three nodules surmounting it. (see Fig. 31); 2 metastatic nodes, 1 cm. in diameter each	Squamous-cell carcinoma, moderately differentiated	8,100 r	6,280 r	28	Severe fibrosis	Tumor destroyed. Well five months
6. G. L. 8/7/44	Extensive tumor incompletely excised. External irradiation given immediately	Adenocarcinoma	7,000 r	4,620 r	48	In 1947 no recurrence in irradiated area, but regrowth of posterior extension into the middle ear and mastoid. Supervoltage irradiation (D <sub>0</sub> , 8,000 r) controlled disease two more years. This latter course of irradiation produced massive necrosis of the auricle, which subsequently was amputated	Death from extension into cranial cavity five years after initial treatment

and one was a squamous-cell carcinoma. Certain radioresistant desmoplastic cylindromatous carcinomas of the parotid are not curable by external irradiation.

On the basis of the aforementioned cases and additional experience with other treatment techniques, the following opinion is ven-

tured: At least 60 per cent of all true cancers of the parotid gland are sufficiently radiosensitive that they can be destroyed with doses of external irradiation which the surrounding normal tissues can tolerate. Other factors will naturally operate to reduce the cure rate of these tumors. The

single-portal-massive-dose technic is an effective means of attacking the disease.

Following are several illustrative cases.

I. J. (Case 2, Table I) had an adenocarcinoma of the parotid. It was removed in 1945, but recurred several months later. A second extensive resection of the tumor failed to remove the deeper portion. Commencing Aug. 25, 1945, a skin dose of 6,900 r was given in thirty-five days to an  $8 \times 10$ -cm. field with 200-kv. radiation. The tumor dose at 4-cm. depth was 4,760 r. The daily skin dose was 300 r. The skin reaction reached a second degree intensity but was healed on the fifty-third day after the first treatment. The patient was free of disease five and a half years later. Commencing three



Fig. 29. Appearance of skin five years after treatment of recurrent, deeply infiltrating adenocarcinoma of the parotid. Irradiation was given immediately following incomplete surgical removal of a recurrent tumor. The skin dose was 7,000 r in thirty-five days. Edema of eyelids is due to lymphatic obstruction caused by radiation fibrosis. No recurrence.

years after treatment, the moderate subcutaneous fibrosis contracted the soft tissues slightly and blocked lymphatic drainage, resulting in moderate edema of the left eyelids (Fig. 29).

J. N. (Case 1, Table I), a Negro, had a conservative excision of an adenocarcinoma of the parotid, moderately differentiated. Six months later there was a local recurrence, and a metastatic node was present measuring  $2.0 \times 2.4$  cm. Commencing Feb. 19, 1947, a skin dose of 8,000 r was given in twenty-eight days to an  $8 \times 10$ -cm. field. The tumor had disappeared by the thirty-fifth day. Skin reaction reached a severe second-degree intensity on the forty-second day but healed on the seventieth day. Two years later, a small portion of the tragus sloughed away, but the defect healed spontaneously. Figure 30 shows the mottled depigmentation and slight fibrosis of the skin, after



Fig. 30. Appearance of skin four years after irradiation of a recurrent adenocarcinoma of the parotid with a metastatic node. Conservative excision had been performed six months previously. The skin dose was 8,000 r in twenty-eight days. One year prior to photograph a small portion of the tragus had sloughed out and the skin had healed.

four years, at which time there was no evidence of recurrence.

L. W. L. (Case 5, Table I) had a rapidly growing, infiltrating, non-circumscribed tumor of the parotid, measuring  $5 \times 6$  cm. (Fig. 31). Biopsy of one of the three small surmounting ulcerating nodules disclosed squamous-cell carcinoma, slightly differentiated. Commencing June 6, 1950, a skin dose of 8,100 r in twenty-eight days was delivered through an  $8 \times 10$ -cm. field, which included two small cervical nodes clinically suspected to be metastatic. The total tumor dose at 3 cm. depth was 6,280 r in twenty-eight days. The tumor was very radiosensitive, shrinking approximately 50 per cent by the fifth day (Fig. 32), and disappearing completely by the fortieth day. The skin reaction reached a third-degree intensity on the thirtieth day and healed completely in two and a half months. Six months after treatment, the skin showed marked depigmentation and fibrosis typical of a third-degree epidermitis. There was slight contracture of the soft tissues of the lobe of the ear (Fig. 33).

The delicate cartilages of the auricle and the soft tissues of the lobe of the ear are severely damaged by large doses of radiation. Massive necrosis occurred in only

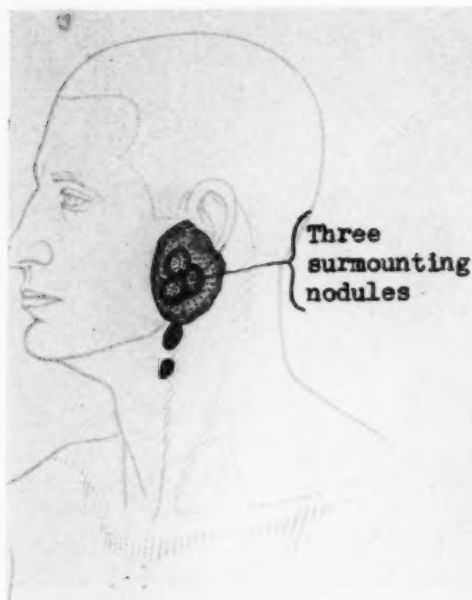


Fig. 31. Squamous-cell carcinoma of the parotid; rapidly growing, infiltrating tumor with three surmounting nodules infiltrating the skin. The skin dose was 8,100 r in twenty-eight days.

one instance (Case 6, Table I). In this case, a marginal recurrence outside the treated area three years after irradiation was treated through a second adjacent field with a skin dose of 8,000 r directly over the auricle. Because of the large dose to two contiguous fields, necrosis occurred.

These massive doses of irradiation caused no injury to the facial nerve. In 3 of the 6 cases, an attempt had been made to remove the carcinoma by radical surgery, and in all 3 facial paralysis resulted.

#### RECURRENT CARCINOMA OF THE BREAST

Although recurrent carcinoma of the breast, on the chest wall, may appear in many forms and may be irradiated with many different techniques, there is one form which can be efficiently irradiated with the single-portal-massive-dose technic. This is the large subcutaneous episternal or parasternal mass which is fixed to the chest wall. Such a lesion arises from subcutaneous residuum or internal mammary node metastasis, and may measure from 4 to 10

cm. in diameter. The tumor lethal dose ranges from 3,500 to 6,800 r in twenty-one to twenty-eight days. The principles of treatment are the same as outlined previously.

In a series of 8 cases, all lesions were destroyed with the single-portal-massive-dose technic. Two patients have survived more than two years after irradiation of a recurrent mass.

#### PRINCIPLES AFFECTING THE CLINICAL APPLICATION OF SINGLE-PORTAL TECHNIC

Routine treatment entails a skin dose of 7,000 to 8,000 r in approximately twenty-eight to thirty-five days in order to deliver the tumor lethal doses illustrated in Figure 28. To begin with, if the tumor extends deeper than 4 cm. from the skin, supplementary irradiation, as indicated above, will be necessary. It should preferably be integrated with external irradiation. Evaluation of the progress of treatment should be made at weekly intervals.

*Seventh Day:* On the seventh day a sharp erythema may portend a hypersensitive skin. A serial biopsy, taken on this day, when the tumor dose is approximately 1,200 to 1,500 r, may be informative. If there are few or no evidences of histologic damage, the probability of failure is high and the treatment may have to be altered. However, final decision can be deferred until the fourteenth day.

*Fourteenth Day:* On the fourteenth day, when the tumor dose has reached approximately 2,500 to 3,000 r, evaluation of the immediate prognosis can be made with some accuracy. A rapid intensification of the epidermitis may suggest poor skin tolerance. Clinical evaluation of the volume shrinkage of the tumor, although not too reliable, may be helpful. For example, if there is 50 per cent shrinkage, the tumor is probably radiocurable, and the maximum eventual lethal dose may be approximately 5,000 to 6,000 r. If the clinical shrinkage in volume is less than 50 per cent, it will probably be necessary to deliver eventually a maximum skin dose of 8,000 r in order to administer a tumor dose

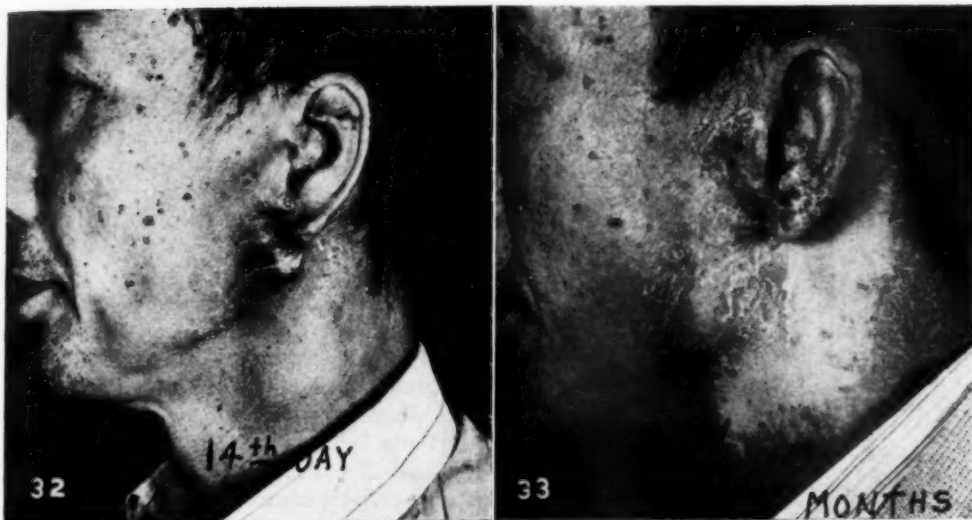


Fig. 32. Fourteenth day. The tumor was radiosensitive, having shrunk 50 per cent by the fourteenth day and completely by the fortieth day.

Fig. 33. Six months later. Severe atrophy and fibrosis of the skin. The dose delivered was probably excessive.

larger than 5,500 r. A serial biopsy taken on the fourteenth day is the most important single index of the response of the tumor to irradiation. Marked acute cell death with disappearance of many of the cells, moderate nuclear aberrations, cytoplasmic swelling, and vacuolation of the remaining cells indicate a satisfactory irradiation effect. If a tumor dose of 3,000 r in fourteen days has produced only 25 per cent volume shrinkage, with no histologic evidence of acute cell death, failure of the treatment can be assumed. In this event there is still time to alter the radiation technic or employ surgical procedures.

*Twenty-first Day:* On the twenty-first day the absence of a second-degree epidermitis indicates a radio-immune skin which should easily tolerate a total skin dose of 8,000 r. In the typical case, the tumor dose is now 4,000 to 5,000 r. Evaluation of volume shrinkage on this day is unreliable. For a good prognosis, the serial biopsy should show disappearance of at least 90 per cent of the tumor cells, and the remaining cells should show marked radiation injury. If the remaining cells, or a small portion of them, show little or no radiation effect, the tumor will probably

recur, regardless of the massive destruction of the greater part of it. One frequently encounters isolated islands of atypically radioresistant cells which behave differently from the major component of the growth. The eventual prognosis is dictated by the most radioresistant portion of the tumor, no matter how small this fraction may be. A useful general rule for serial biopsies is: After all tumor cells have disappeared histologically, whatever the dose may be, an additional 1,000 r should be given.

#### RESULTS WITH SQUAMOUS-CELL CARCINOMA OF THE UPPER RESPIRATORY TRACT

The purpose of this preliminary report is to describe a specific technic and to indicate its probable efficiency. Too few patients have been followed long enough to provide a five-year cure rate. Furthermore, during the war years, many cases were lost to follow-up study.

Almost all cancers treated with the single-portal-massive-dose technic were moderately advanced or advanced lesions, with a high incidence of metastasis. Twenty-four patients whose *primary tumor* was irradiated with this technic have been





Fig. 34. Extrinsic carcinoma of the larynx. Photograph was taken two years and a half following a skin dose of 7,800 r in fifty-one days to a large recurrent fixed node at the angle of the jaw, measuring  $4 \times 6$  cm. Six months prior to this recurrence, a total laryngectomy and left radical neck dissection had been performed for an extensive carcinoma of the epiglottis and vestibule with a large metastatic node in the lower cervical region. Radiation sequelae were mild. At present there is no evidence of disease. The fullness at the angle of the jaw is soft, doughy fibrosis.

followed for six months to five years. Fifteen patients are free of disease from six months to five years, 6 of these for two to five years. Nine patients died, 2 from distant metastases, the primary tumor having been controlled. In retrospect, it is seen that many failures occurred with lesions deeper than 4 cm. from the skin, wherein supplementary irradiation to the deep part of the tumor was given as an afterthought or for later recurrence, rather than as an integral part of the original course of irradiation.

The effect of this technic against *cervical nodes* was more favorable than against the primary tumor, probably because their superficial location permitted a satisfactory tumor lethal dose. Twenty-six patients with metastatic nodes were irradiated. In

most instances, the diagnosis was made clinically. The authors were hypercritical in offering a clinical diagnosis of metastatic cancer in the case of an enlarged, hard lymph node. Many questionable nodes were not considered metastatic. It is possible that some nodes called metastatic may have been inflammatory. Of the 26 patients with metastatic nodes, 9 are known to be dead; of these, 6 died from remote metastasis without recurrence of the nodes. Thus, metastatic nodes were controlled in 23 of 26 patients. Seventeen patients who had metastatic nodes are alive and free of any disease for six months to five years, 6 of these being alive for more than two years. The disparity between the figures for metastatic nodes and primary tumors is due to inclusion of a number of patients whose primary tumor had been controlled previously and who presented themselves for treatment because of recurrent metastatic nodes (Fig. 34).

#### DISCUSSION

Most radiologists have relinquished metastatic cervical nodes to radical surgical dissection. Interstitial irradiation can destroy many accessible and superficial nodes (5), but can seldom bring about the destruction of deeply situated nodes, particularly small nodes in contact with great vessels or large nodes which have infiltrated the deep structures of the neck. The single-portal-massive-dose technic is capable of destroying these nodes.

Ellis (6) and Paterson (7) have defined a skin-tolerance dose based on certain minimal late skin changes. This might preferably be designated "minimum tolerance dose." The authors' experience with larger skin doses implies a corollary definition of "maximum tolerance dose," which produces changes on the threshold of necrosis. With this principle a greater number of lesions can be brought into the range of radiocurability.

Obviously, with a single portal, the disease is not uniformly irradiated. This is often fortuitous in that the more radio-resistant cervical nodes (Fig. 28) receive a



larger tumor dose than the primary tumor because of their superficial location.

#### CONCLUSIONS

1. The single-portal-massive-dose technic for fractionated external irradiation satisfies the physical and clinico-biological characteristics of certain laterally situated cancers of the upper respiratory tract, salivary glands, and recurrent breast carcinomas. It delivers the required tumor lethal dose to the primary tumor and nodes in proper proportion more effectively than cross-fire technic and with less discomfort to the patient. It was employed in 74 cases.

2. Its disadvantages are: reduced effectiveness for tumors deeper than 4 cm. from the skin, and the severity of the skin reactions and their potential sequelae (one instance of early necrosis and one of late necrosis, the latter occurring when 1,000-kv. radiation was employed).

3. The skin can tolerate a dose of 8,000 r delivered over a period of five weeks or longer to a field measuring approximately  $8 \times 10$  cm. This portal includes the primary tumor as well as metastatic nodes. The quality of the beam of irradiation is 1.0 to 2.0 mm. Cu h.v.l.

4. The single-portal-massive-dose technic increases the potentiality for radiocurability of certain squamous-cell carcinomas and their metastatic nodes. Its beneficial

effect on parotid cancer brings that lesion from the realm of surgery into that of radiation therapy. It is an effective technic for the treatment of bulky chest wall recurrence of breast cancer.

5. The tumor lethal doses for squamous-cell carcinoma of the upper respiratory tract have been more clearly defined as a result of these experiences.

ACKNOWLEDGMENTS: Patients were treated at New York University Hospital, Hospital for Joint Diseases, Bellevue Hospital, Halloran VA Hospital, and Walter Reed General Hospital. Photomicrographs were made at Armed Forces Institute of Pathology, Washington, D. C.

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#### SUMARIO

#### Técnica Roentgenoterapéutica de Dosis Masiva y Puerta Unica para Ciertos Cánceres de las Vías Aéreas Superiores, la Parótida y Recurrentes de la Mama

La técnica descrita de dosis masiva y puerta única es para la irradiación externa fraccionada de ciertos tumores laterales de las vías aéreas superiores y las glándulas salivales y del carcinoma mamario recurrente. Básiase en la tesis de que la piel de dichas regiones puede tolerar una dosis irradiatoria hasta de 8,000 r, administrada en cuatro a cinco semanas por una sola puerta que mida unos  $8 \times 10$  cm., y que abarque tanto la lesión primaria cuanto las

metástasis ganglionares. Esa técnica posee la ventaja de entregar a los ganglios más superficiales una dosis proporcionalmente mayor que la entregada al menos radorresistente tumor primario.

Setenta y cuatro enfermos fueron tratados con esta técnica. La dosis cutánea diaria varió de 300 a 400 r, que se proponía introducir una dosis tumor media diaria de 225 a 275 r. La dosis cutánea total óptima fué de 7,000 a 8,000 r, administrada

en cuatro o cinco semanas. La calidad de la irradiación varió de 1.0 a 2.0 mm. de capa de hemirreducción de cobre, excepto en 4 casos tratados con 1,000 kv. (c. h.-r. 10 mm. de cobre).

La técnica se reserva para tumores que queden a una profundidad no mayor de 4 cm. de la piel. Otra desventaja consiste en la posibilidad de que sobrevengan intensas reacciones cutáneas y hasta esfacelo en alguna que otra piel atípicamente radiosensible. En la mayoría de los casos, obsérvense, al cabo de uno o dos años, pronunciada atrofia, desvascularización y espe-

samiento en tabla de la piel y los tejidos subcutáneos.

Esta técnica parece acrecentar las potencialidades de radiocurabilidad de ciertos carcinomas escamocelulares y de las metástasis ganglionares de los mismos. Su efecto beneficioso en los tumores de la parótida traslada esas lesiones del reino de la cirugía al reino de la irradiación. También constituye una técnica eficaz para las recurrencias voluminosas del cáncer mamario en la pared torácica. Ha servido además para definir con mayor exactitud la dosis tumor letal en las neoplasias de las vías aéreas superiores.

#### DISCUSSION

**Harold W. Jacox, M.D.** (New York): This afternoon we have had two directly opposite therapeutic technics presented, one which makes use of the greatest number of portals possible in a given plane, as pointed out by Dr. Trump<sup>1</sup>—in other words, rotation therapy—and the other which uses a single portal. As the old saying goes, "You pays your money and you takes your choice."

If carried out as recommended, this latter method has definite but limited usefulness. I converted the skin doses to the more familiar ones measured in air and found that the optimum daily dose as given by Drs. Friedman and Davis varies from 230 to 265 r in air, with the size field employed. The total dose, which was 8,000 r measured on the skin, ranges from 5,280 to 6,080 r measured in air, depending upon whether the half-value layer is 1 or 2 mm. of copper. The total volume of tissue to be irradiated is 320 c.c., as you may recall—an 8 × 10-cm. field and a 4-cm. depth—but of course this is not uniformly irradiated, as Dr. Trump's diagrams would certainly show.

One thing Dr. Friedman did that I think was fine; he showed not only good results but also some of the bad ones.

I agree with the authors about confining irradiation to one side of the head or neck when unilateral disease is present. I see no reason, however, why multiple convergent beams, not necessarily opposing or large ones, which will produce the same or an even greater and more homogeneous tumor dose, may not be used with less danger of cutaneous and osseous breakdown at a later date. I admit that the patient will

not die of these changes, and plastic surgery is a wonderful help, but if we can avoid severe damage, I think we should try.

It has often been difficult for me to determine the exact extent and depth of infiltration of many neoplasms, as I suppose it has been for you, so that I have tried to hit them from as many angles as possible. I think this suggests one of the drawbacks of the method just presented.

I have used this technic in a few selected cases and have found it definitely worth while. I think we all, as radiologists, should keep it in mind for certain selected cases.

**Dr. Friedman (closing):** As was stated in presenting our results, there were a number of deaths, including an Army officer whose case will be described in detail in our paper as it will appear in *RADIOLOGY*.

This patient was used to illustrate the healing of the skin reaction and the interesting serial biopsies. Actually, his recurrence was at the posterior superior margin of the tumor, which was more than 4 cm. from the skin, where the fall-off in dose was such that less than the necessary tumor lethal dose was delivered.

Multiple beams are useful for bulky neck nodes, but not against small nodes which overlie a primary tumor. These nodes are the ones which we undertake to irradiate with the simple single-portal technic.

Comparable to this technic is that employed by Dr. Frank Ellis, with the wedge filter. He undertakes to accomplish a dispersion of irradiation in tissue similar to that obtained by us.

Dr. Jacox mentioned two drawbacks to this technic: one was the lack of uniformity. We

<sup>1</sup> See Hare, Trump, et al.: *Radiology* 57: 157-167, August 1951.

are using an obviously non-uniform distribution of radiation in depth, accomplishing certain results. The more superficial tissue receives a larger dose. This is necessary to destroy the more resistant nodes. The deeper tissues, containing the more sensitive primary tumor, receive a smaller dose. The further drawback of difficulty in measuring the exact depth of the tumor is well known to us. That can be overcome somewhat by careful observation of the

shrinkage of the deeper portion of the tumor and by serial biopsies from the deepest part.

The one significant contribution of this technique is that it brings parotid cancer back from the realm of surgery into that of radiation therapy.

Finally, I agree with Dr. Trump's thesis, that with supervoltage radiation not only can the same results be accomplished, but probably superior results. The point is that our results were achieved with 200 and 250 kv.



# End-Results in the Treatment of Ovarian Carcinoma with Surgery and Deep X-Ray Irradiation<sup>1</sup>

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THE FIVE-YEAR survival rate for primary ovarian carcinoma has been fairly constant. This is due to the insidious onset of the disease and the lack of characteristic or alerting symptoms. By far the most common complaint on the part of the sufferer is enlargement of the abdomen or a mass arising in the lower pelvis. Other symptoms, such as leukorrhea, vaginal bleeding, or pressure signs are usually disregarded by the victim, and as a result patient delay is the primary reason for poor end-results. Recognizing this fact in the treatment of those patients who were admitted to our service at the Mercy Hospital Institute of Radiation Therapy (Chicago), we have endeavored to analyze a group of 143 cases, 113 of which were treated initially by the senior author (H. E. S.). These cases have been observed for at least five years following therapy. Contact was lost with 13 of the patients and we have been unable to obtain information as to their progress. They are therefore counted as deceased in the final tabulations.

## SYMPTOMS

Because of the insidious onset of ovarian carcinoma, the early stage is frequently unrecognized by the patient and by the physician as well. In reviewing the symptomatology, an effort was made to determine the cardinal symptom in each case. A not too surprising observation was that most individuals complained of symptoms which appear late in the disease. The majority stated that abdominal swelling was their first indication of difficulty, while many complained of an abdominal mass.

TABLE I: OVARIAN CARCINOMA: CARDINAL SYMPTOMS

Cardinal Symptom	Cases	Per Cent
Abdominal swelling.....	65	45.4
Abdominal mass.....	28	19.6
Feeling of abdominal weight.....	9	6.3
Weight loss.....	19	14.0
Vaginal discharge.....	20	14.9
Urinary symptoms.....	9	6.3
Diarrhea, etc.....	12	8.3
Menstrual irregularity.....	20	14.9
Not known.....	15	10.4
No symptoms.....	7	4.8

An ovarian neoplasm large enough to produce recognizable swelling of the abdomen has usually filled out the true pelvis and, if palpable by the patient, is approximately three to four months gestational size. Although certain histologic types of malignant ovarian neoplasms grow rapidly, a lesion of the most active growth type must have been present for three to six months to reach such dimensions. In some cases where the opportunity to check the rate of growth was afforded by patient delay after discovery of the tumor by her physician, twelve months or longer were required for attainment of this size. As the tumor grows, it encroaches on other structures in the confines of the pelvis and frequency and urgency of urination result. If the pressure within the pelvis is adequate or if the disease process directly invades the ureters, interference with kidney function occurs. The vaginal discharge may be coincidental. Menstrual irregularity and postmenopausal bleeding do occur and are for the most part the result of pelvic hyperemia due to the neoplasm and not to hormonal influences, except in the hormone-producing neoplasms. One possible conclusion is that the symptoms, as a rule, appear late in the disease and cannot be relied upon to warn the patient or the physician of the presence of

<sup>1</sup> Read before the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 10-15, 1950.

the neoplasm at a time when treatment would be most effective. Frequent and thorough pelvic examination of all patients under our care is the only means of discovering these neoplasms early.

In Table II we have shown the time elapsing between recognition of the first symptom by the patient, as described in her detail of events, and the day of her first consultation with a physician.

TABLE II: OVARIAN CARCINOMA: DURATION OF SYMPTOMS BEFORE MEDICAL ADVICE WAS SOUGHT

Length of Time	Cases	Per Cent
Under 1 month.....	34	23.7
Under 2 months.....	17	11.8
Under 3 months.....	8	5.5
Under 4 months.....	7	4.8
Under 5 months.....	6	4.1
Under 6 months.....	9	6.3
Between 6 and 9 months.....	1	0.07
Between 9 and 12 months.....	0	0.0
Between 1 and 2 years.....	10	6.9
Over 2 years.....	15	10.4
No signs.....	8	5.5
Not known.....	28	19.6

Only 23.7 per cent of the patients consulted a physician within one month, while 17 (11.8 per cent) sought medical aid within the second month. A startling number, 15 (10.4 per cent) to be exact, allowed two or more years to elapse before seeking advice and treatment. Needless to say, in all of these unfortunates the disease was terminal on their initial visit. The only commendable observation is that in 8, or 5.5 per cent, the lesions were discovered through routine office procedures. When we reflect that in all malignant neoplasms the extent of the growth is more important than the cell type in influencing the recovery rate, we realize that here is one instance where detection examination and lay education need increased support.

Table III encourages us by disclosing that the physician is alert and cognizant of the importance of early diagnosis in fulfilling his part in obtaining immediate and proper treatment for his patient. In only a few instances was he responsible for delay, and this usually due to complacency while he awaited development of a more characteristic or impressive symptom. A

TABLE III: OVARIAN CARCINOMA: INTERVAL BETWEEN OBSERVATION BY A PHYSICIAN AND DIAGNOSIS

Length of Time	Cases	Per Cent
Under 1 month.....	116	81.1
Under 2 months.....	15	10.4
Under 3 months.....	4	2.8
Under 6 months.....	4	2.8
Under 12 months.....	3	2.0
Under 2 years.....	1	0.07

patient thirty-five years of age and over should have a pelvic and rectal examination as part of her physical evaluation no matter what her complaint may be, unless such a procedure has been satisfactorily carried out within the previous three months. In reviewing these cases, we find that out of 143 cases, 116 were diagnosed within one month, and in 15 cases the diagnosis was delayed for two months. A distressing observation is that in 12 (9 per cent) individuals it was more than two months after the physician was seen that the pathological entity was discovered.

We can assume from the foregoing figures that proper strides are being made in the field of ovarian carcinoma. There is still need, however, for education not only of the patient but also of the physician.

#### AGE INCIDENCE

Ovarian carcinomas seemingly affect those in middle life, and the consensus of opinion is that the varieties of tumors that occur in the various age brackets are coincidental. The youngest patient in this series was only sixteen, while the eldest was eighty-two years of age.

TABLE IV: AGE INCIDENCE OF OVARIAN CARCINOMA

Age Groups	Cases	Per Cent
Under 20.....	2	1.4
20-30.....	7	4.8
30-40.....	24	16.6
40-50.....	37	25.8
50-60.....	40	29.8
60-70.....	17	11.7
70-80.....	3	1.6
Unknown.....	13	9.0

The girl of sixteen, who is still living, had an embryonic type of tumor, a dysgerminoma; while the eighty-two year old patient presented herself with a disseminating type of adenocarcinoma and went



rapidly downhill. The peak of age incidence in our series was in the sixth decade. Meigs, Montgomery, and others have also found the highest percentage of cases in the sixth decade. The drop in the seventh and the eighth decades may be attributed to a decrease in the number of persons who, under any conditions, would be alive at those ages, rather than to a lower susceptibility to the disease in later life.

#### PATHOLOGY

Before proceeding further, it may be profitable to direct our thoughts to a brief résumé of the gross pathology involved in ovarian cancer. Pathologically the tumors can be divided into two categories, solid and cystic growths. The entirely solid and the partially cystic carcinomas are by far the most serious. These tumors grow as medullary, scirrhous, squamous, adeno- or papillary adenocarcinomas. The cell type may be pseudomucinous, endometrial, or unclassified. The solid type of tumor is devoid of cysts, except those resulting from necrosis. The walls are thick and invaded by cancer cells, and large carcinomatous masses are present in the cysts, which are due to marked necrosis and liquefaction. These tumors may be small or massive. Their general contour is round or ovoid, the surface smooth, and the color on cross section is grayish or grayish pink. The consistency varies according to the proportions of epithelial and fibrous elements present. In most medullary varieties, the tissue is soft and brain-like; while in the scirrhous type, it is hard.

The origin of the cystic tumors is still debatable. Some authorities, including Ewing, divide them into two groups, maintaining that the neoplasms of one group originate in previously benign cysts, while those of the second group begin as primary cystic carcinomas. Meyer and Novak believe that primary ovarian carcinomas, as such, do not occur; they maintain that the malignant type is invariably the result of a carcinomatous change in a previously benign cyst.

The gross characteristics of the cystic

variety are similar to those of the benign pseudomucinous cyst. In a portion of the tumor, often sharply circumscribed but occasionally extensive, one finds firm knobby areas which when opened reveal a spongy mass with a considerable amount of gelatinous material. The fluid varies in consistency; it may be thick and gelatinized, thin and watery, or hemorrhagic. In other ovaries, however, there remains no trace of a benign cystadenoma, and the entire area is made up of carcinomatous tissue.

The cystic tumor is not as malignant as the solid. The unclassified cell type is the least serious, the pseudomucinous next, while the cyst with areas of adenocarcinoma carries the poorest prognosis.

#### EXTENSION

It is generally concluded that the extension of the neoplastic process occurs by one of two methods: (1) *via* the lymphatic channels and (2) by implantation in the peritoneal cavity by direct contamination. The process begins generally, it is thought, in the medullary portion of the ovary. The tunica of the organ offers a substantial barrier, for a period, to the outward progress of the growth. If the tumor is of the papilliferous variety and the capsule of the ovary has been overcome, direct implantation occurs. In the malignant cysts, one can visualize the papillae gradually encroaching upon the fluid content and expanding to the point of rupture. The adjoining tissue then becomes carcinoma-soiled. If the ovary contains a solid carcinoma, the growth takes place by direct extension.

Invasion and spread through the lymphatic chain is usually a late phenomenon. It is conceivable that there may be some propagation *via* the blood stream, but this is rare.

#### CLASSIFICATION

The clinical grouping of these tumors has been a controversial issue. Various groupings have been advocated, and though they may be in essence the same, they still tend

to confuse the reader by their multiplicity. In this series, the Schmitz classification has been used. Briefly it is as follows:

*Group I:* Tumor completely operable, affecting only one ovary; not adherent and not extending to surrounding tissue.

*Group II:* Tumor completely operable, affecting the ovaries unilaterally or bilaterally; may be adherent or extend into the surrounding tissues.

*Group III:* Tumor completely inoperable, though partial removal may be done; extension into adjacent tissues.

*Group IV:* Extensive tumor, invasive and producing metastases. In this group are placed those cases in which only an exploratory operation or biopsy can be performed.

*Group V:* Tumors inoperable and terminal.

#### END RESULTS

The management of the patients in our series included both irradiation and surgery. All but 2 received roentgen therapy. Radium was inserted in 2 cases, with no immediate results. Of the 143 patients, 105, or 73.4 per cent, received beneficial extirpating surgery. In 16 cases, approximately 11 per cent, an exploratory procedure was done, and in 13.2 per cent there

TABLE V:  
OVARIAN CARCINOMA: FIVE-YEAR SURVIVALS

Grouping	Total Cases	Five-Year Survival	Per Cent
Group I	40	11	27.5
Group II	26	9	34.6
Group III	13	5	20.0
Group IV	26	4	15.3
Group V	38	0	0.0
TOTAL	143	29	20.3

was no surgical intervention, because the patient could not withstand the procedure or was beyond surgical aid. The five-year survival rate is 20.3 per cent, which conforms to the results of others.

If we eliminate in the final tabulation those cases in which only supportive therapy could be instituted because of advanced disease, 38 cases in all, we would

TABLE VI: OVARIAN CARCINOMA: SURVIVAL PERIODS

Survival Time	Cases	Per Cent
Under 1 year	62	43.35
1 to 2 years	10	6.99
2 to 3 years	11	7.69
3 to 4 years	6	4.19
4 to 5 years	3	2.08
Over 5 years	29	20.28
Untraced	22	15.38
TOTAL	143	100.00

have a corrected survival percentage of 27.5 per cent. Table VI gives us the survival rate in months for the entire series.

In reviewing Table V, we can see that the highest survival percentage is where "cure" is most expected, in Groups I and II. In the microscopic segregation of those cases which have reached the five-year mark (Table VII), we find that the majority, 17, or 58.5 per cent, are of the cystic variety: 14 of the papillary cystadenocarcinomatous variety and 3 pseudomucinous adenocarcinomas. In this five-year survival table, we have chosen to include our one case of granulosa-cell tumor.

TABLE VII: OVARIAN CARCINOMA: FIVE-YEAR SURVIVALS FOR VARIOUS TYPES

Type of Tumor	Cases	Per Cent
Papillary cystadenocarcinoma	14	48.2
Pseudomucinous adenocarcinoma	3	10.3
Adenocarcinoma	7	24.1
Medullary carcinoma	1	3.3
Dysgerminoma	1	3.3
Granulosa-cell	1	3.3
Myxosarcoma	1	3.3
Unclassified	1	3.3

There exists some controversy as to the true picture of malignancy in this variety, since microscopically it appears at times to be benign. However, malignant tendencies have frequently been noted.

#### DISCUSSION

When ovarian tissue is suspected of malignancy at the operating table, radical and extensive surgical procedures should be carried out. A total hysterectomy is definitely preferred to the subtotal procedure. It is also worth remembering that carcinomas may develop in small rests of benign pseudomucinous cysts which are left behind, as can so readily happen when

cysts are extensive and adherent or ruptured. This explains why, long after operation for a cyst which has been reported as benign, the patient may return with a carcinomatous mass in the peritoneal cavity.

When carcinoma has been discovered in one of the ovaries, a pressing question immediately arises demanding an immediate answer. Should the other ovary be removed? An embarrassing situation may be imposed under these conditions, namely, extirpation of one seemingly benign ovarian cyst, with a microscopic report, five or six days later, of carcinoma.

The dictum that has been observed is that bilateral oophorectomy should always be done in justice to the patient. Mary Moench stated that in her series of patients with initial unilateral involvement, and unilateral oophorectomy, 22.2 per cent later died of carcinoma of the other ovary. Norris and Murphy reported similar findings, namely, that 17.5 per cent of grossly benign appearing ovaries proved on examination to be malignant. Meyer gives a higher and a more striking figure, stating that 50.5 per cent of ovarian cancers are bilateral. Diddle leads the opposition, stating that the normal ovary is often removed unnecessarily and suggesting that unilateral resection be considered in young women. We, on the other hand, are of the opinion of Cashman and Helsel, who state that age should not be considered in the treatment of ovarian carcinoma. The only exception to the rule is when the offending lesion is of the granulosa-cell type.

Most ovarian tumors are resistant to irradiation, and it should never be employed as a substitute for surgery, but enough evidence has been compiled to adjudge it as a definite asset in the therapy of this disease. Controversy exists, however, even on this latter point. TeLinde and others do not feel that statistical results justify routine roentgen therapy postoperatively. On the other hand, Taylor and Greeley, Kerr and Einstein, and Jacobs report excellent results with irradiation.

The policy followed in this series was to extirpate as much diseased tissue as possible and follow with x-ray therapy. Irradiation employed by different authors has varied slightly so far as physical factors are concerned. Our plan is as follows: 800 kv.; 10 ma.; 70 cm. F.S.D.; filters Pb 1.0 mm., Sn 1.56 mm., Cu 2.62 mm., Al 3 mm.; extension chamber 2 mm.; half-value layer 3.0 mm. Cu. The depth dose at 10 cm. is 56 per cent; 250 or 300 r are administered daily, and the number of fields is regulated by the measurements of the patient. A total tumor dose of 4,500 to 5,000 r is given.

As mentioned previously, the value of postoperative irradiation has been established. Crainz and Schmiemann state that an increase in the five-year survival of 0 to 20 per cent can be obtained, and Taylor and Greeley showed almost 100 per cent improvement with irradiation in their series. The results in our cases of malignant neoplasms compare favorably with those of others reported in the literature.

#### SUMMARY

A review of 143 cases of malignant ovarian neoplasms failed to reveal a characteristic symptom which would indicate to the patient or her physician the possible presence of such a lesion in its incipency. Abdominal swelling or the presence of a mass was the observation that brought 65 per cent of this group for diagnosis. It is estimated that three to six months will have elapsed before sufficient size to produce recognizable abdominal enlargement is attained by the most active of such growths, and at least twelve months by the less malignant tumors. By this time extension to the peritoneal surfaces and omentum is usual, and such extension influences the survival rate adversely. In spite of the lack of characteristic early symptoms, there are disturbances that indicate disease, but they are so mild as usually to be ignored or credited to the "period of life" of the individual. Routine pelvic examination at frequent intervals seems to offer the only solution to the problem of early diagnosis.

With surgical removal of the entire uterus, both tubes and ovaries, plus the omentum, followed by intense roentgen irradiation of the entire pelvis, the five-year survival in this group of patients was 20.28 per cent. If we eliminate all cases which had progressed beyond the stage where complete surgical removal of the gross disease was possible, the survival rate is in the neighborhood of 50 per cent. The future outlook for these sufferers is brightened by our knowledge of the efforts of physicians throughout this land of free medical enterprise to discover cancer in an early stage.

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## SUMARIO

### Resultados Terminales en el Tratamiento del Carcinoma Ovárico con la Cirugía y la Roentgenoterapia Profunda

El repaso de 143 casos de neoplasias malignas del ovario no reveló el menor síntoma típico que indicara la posible presencia de dicha lesión en su incipiente. Cálculase que transcurrirán de tres a seis meses antes de que alcancen tamaño suficiente para producir dilatación reconocible del abdomen los más activos de esos tumores, y por lo menos doce meses tratándose de los menos malignos. Para esa época, lo habitual es difusión a la superficie del peritoneo y al epiplón.

Con la extirpación quirúrgica de todo el útero, con las trompas y ovarios, y además el epiplón, seguido esto de la intensa irradiación roentgenológica de toda la pelvis, las sobrevivencias de cinco años en este grupo de enfermas llegaron a 20.28 por ciento. Eliminados todos los casos que habían avanzado más allá del periodo en que era factible la completa extirpación quirúrgica de la enfermedad macroscópica, la tasa de sobrevivencias se aproxima a 50 por ciento.



## Role of Surgery in the Management of Cervical Carcinoma<sup>1</sup>

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CANCER OF THE cervix uteri has been the subject of intensive investigation from time immemorial. Gradually over a period of years, the increasing knowledge of the physics of radiation and the improvement in irradiation technic have established roentgen therapy as the most effective procedure for this type of malignant growth. The status of the matter is not, however, settled or stationary, since improvement in surgical technic has influenced sound clinicians to re-adopt the operative treatment of cervical carcinoma. In spite of the present-day controversy, irradiation remains the basic method of treatment, but surgery is unquestionably a necessary adjunct in some selected cases. Consideration of the surgical indications and procedures is the purpose of this discussion, with a view to suggesting to the radiotherapist a possible source of help in salvaging some cases that might otherwise be lost and in improving results in such conditions as pre-invasive carcinoma, resistant carcinoma, and carcinoma in pregnancy. Palliative surgery will also be considered.

### PRE-INVASIVE CARCINOMA

The term "pre-invasive carcinoma" denotes a carcinoma which is confined to the natural surface and does not penetrate the underlying stroma. An accurate diagnosis of true intra-epithelial cancer may, however, be difficult to make. Evidence as to non-invasive biologic characteristics obtained by performance of a single biopsy may be erroneous. To minimize the error, a careful study of several sections must be undertaken. Not infrequently cases interpreted as pre-invasive on single biopsy examination have been found to show true invasive properties when further areas were

studied. Biopsy at four points, at least, on the cervix and a scraping of the endocervix must be done to produce reliable evidence of non-invasion. Only serial sections of removed specimens enable the clinician to make the diagnosis with finality. Some investigators maintain that a definite hazard exists in the promotion of distant metastases by diagnostic tissue excision and advise a clinical attempt at diagnosis for all cancer groups without biopsy examination. Paterson and Nuttall, in an attempt to throw light upon this question, compared the incidence of metastases in two groups of patients with comparable cervical cancer, one with biopsy and one without. In a series of 166 cases (99 with biopsy; 67 without) they found the incidence of metastasis to be slightly higher in the group in which biopsy was not done.

The necessity of differentiating between the pre-invasive and the invasive carcinoma lies in the significant difference in their treatment. It is generally agreed that the cure rate of early cancers of the cervix which are treated with radiation approaches 80 to 90 per cent. Irradiation in the pre-invasive group, however, is not ideal, since the average age of these patients is between thirty-six and thirty-seven years. In our clinic, total hysterectomy has been found to be adequate for such cases, thereby preserving the gonadal function and avoiding secondary changes in the pelvis and genital tract, which are undesirable in young women. Hoge reports, in a survey of treatment of carcinoma *in situ* in the United States, that total hysterectomy is the most favored procedure in the majority of the leading clinics of the country. More conservative measures, as amputation, conization, or cauterization,

<sup>1</sup> Read before the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 10-15, 1950.



have been utilized in the treatment of lesions presumed to be intraepithelial in nature, but such therapeutic procedures invite disaster in cases in which invasive characteristics have been overlooked on microscopic examination. Total hysterectomy, on the other hand, will suffice for an extremely early invasive lesion, and, if the serial microsections show an invasive pattern, subsequent radiation treatment may augment an otherwise inadequate operation.

Since it has been definitely proved that the end result of any form of therapy depends primarily upon the clinical extent of involvement rather than the histologic grading of the malignant process, it is essential that all patients be clinically grouped before therapy is discussed. This enables various investigators to compare different methods of treatment for identical stages of the disease. We prefer the Schmitz classification, because of its simplicity and ease of application. It is extensively utilized in American clinics and will continue to be used as a working diagnosis after the establishment of an international classification. Its chief advantage is the opportunity to study the results in treatment of early invasive lesions.

*Clinical Group I:* A freely movable uterus, as determined under anesthesia, with a proliferating or ulcerating lesion up to 1 cm. in diameter and confined to the cervix. This includes any lesion from the earliest microscopic evidence of invasive carcinoma, but should not include pre-invasive lesions, which are best regarded as a separate group until more is known of their behavior. This group we designate as the clearly localized cancer.

*Clinical Group II:* Ulcerative or proliferative lesions above 1 cm. in circumference, up to those involving the entire cervix but not invading the paracervical areas, vaginal tube, or parametrial tissues. Edema is often present in the paracervical areas, but there is no definite evidence of invasion. Probably 20 per cent of this group of patients have undiagnosed lymph node invasion. This is called the doubtful

group, as doubt exists as to the localization of the disease to the cervix.

*Clinical Group III:* Lesions of varying size with definite extension onto the vaginal cuff, but limited to the upper half of the vaginal tube, and into the paracervical areas and parametrial tissues. Although this extension is most frequently lateral, it may be anterior into the vesicovaginal septum or posteriorly along the sacrouterine ligaments or rectal tissues. There is not complete fixation of the pelvic tissues, but the disease may have spread to the bony pelvis without fixation. This is the truly invasive stage.

*Clinical Group IV:* Bladder invasion, rectal invasion, parametrial fixation and distant metastases; hopeless fixed cancer.

#### RESISTANT CANCER

Within the past few years there has been a rekindling of interest in the radical operation of hysterosalpingo-oophorectomy combined with lymphadenectomy, for the treatment of certain early selected cases. Meigs, who until recently, enthusiastically employed this method, restricted its use to good operative risks with involvement of not more than the cervix, and without invasion of the parametrium. One of the principal contentions submitted by the adherents of the surgical school in support of their radical approach involves the question of unrecognized lymph node involvement in cases erroneously classified as Group I or II. They reason that cancer cells within lymph nodes become radio-resistant, and that this would account for the failures in the early cases. On this premise the patient would survive by virtue of lymphadenectomy. This conclusion, we feel, is not valid, since Morton found positive nodes in 39.3 per cent of a series of carcinomas treated by the Wertheim procedure but not irradiated, and only 11.4 per cent in a group receiving preoperative irradiation. This demonstrates that lymph node metastases are not only responsive to irradiation but may be effectively eradicated. Meigs, in a recent report on the first 75 of his cases subjected

to radical surgery, shows 78.7 per cent good five-year end-results. Of the 16 patients that died, 10 (80 per cent) had lymph node involvement at operation; while the incidence among the 59 patients that survived was only 7 per cent. This represents an 18.6 per cent incidence of lymph node involvement in a selected group all classified as League of Nations Stage I. In other words, 71.3 per cent of the patients with lymph node involvement died, which serves to *de-emphasize* the value of surgery in the management of this complication.

Generally, the relative merits of radical surgery as the sole treatment of carcinoma of the cervix apply only to cases falling within Groups I and II (Schmitz classification). The surgical procedures utilized in these early cases include the Wertheim operation with pelvic lymphadenectomy, or modifications thereof, as well as the Schauta hysterovaginectomy, depending upon the indication in the individual case. Another group of cases lending itself to surgical consideration is that in which the primary lesion is determined to be radio-resistant subsequent to therapy. In this group, failure to respond to radiation therapy, as demonstrated by repeated biopsies or cytologic studies, together with the clinical evidence of failure in the form of progressive infiltration or absence of regression, is sufficient indication for resort to surgical intervention. In our experience, cell types that do not respond to the initial course of irradiation will show little improvement if further radiation is administered.

Our selection of cases of early cervical cancer for operative treatment is confined to the following groups:

1. Radioresistant cell types as proved by repeated biopsies, cytologic studies, or clinical evidence during or after irradiation therapy
2. Complete prolapse of the uterus, complicating Groups I and II
3. Pregnancy
4. Refusal of radiation therapy by the patient.

Prolapse of the uterus, because of the intrinsic anatomical derangement, greatly interferes with the intelligent application of radiation therapy. The commonly employed procedure was developed principally by Schauta and includes vaginal hysterectomy plus a wide removal of the parametrial tissues and a cuff of the vagina. Schuchardt's paravaginal incisions can be employed to facilitate and enlarge the operating field.

Read believes that the presence of large myomata or ovarian cysts complicating cervical cancer may warrant surgery, since these complications can, in rare instances, preclude the application of adequate radiation therapy.

#### CANCER IN PREGNANCY

In the clinical situation of carcinoma of the cervix with an associated pregnancy, treatment must be guided by the stage of gestation. Carcinoma of the cervix detected in the first trimester of pregnancy is subjected to intensive therapy without regard to the gestation. When the disease is found in the second trimester, deep x-ray therapy to check the carcinomatous growth is generally employed until the period of viability is reached. Our formulated plan of therapy for this complicated situation is to deliver the child by cesarean section when viability is attained, thereby avoiding cervical trauma and possible hemorrhage attendant upon vaginal delivery.

The wisdom of this plan seems to be substantiated by Heyman, who showed that of patients in whom an induced abortion or Porro section was done prior to irradiation, only 11.1 per cent survived five years with no evidence of disease, while subsequently, in a group of cases in which radiation was used and spontaneous abortion permitted, a 57 per cent five-year survival rate was obtained.

Although some authors advocate pan-hysterectomy at the time of the cesarean section, the technical difficulty, due to the vascularity of the pelvis, does not justify the risk. It seems to us that, with preservation of the corpus uteri, prompt in-

stitution of x-ray therapy followed by radium application after involution may aid in preventing widespread recurrence. If the lesion fails to respond to irradiation or is found histologically to be radioresistant, the ultimate recourse is the radical surgical procedure.

#### OPERATIVE PROCEDURES

Thus far the discussion has been limited to the carefully selected cases that are placed in the so-called "operable group," that is, Groups I and II (Schmitz). In spite of this high degree of selectivity, the results obtained by irradiation are extremely hard to duplicate.

#### Results with Irradiation, 1933-1945

Clinical group.....	I	II	III	IV	Total
Number admitted....	14	44	79	51	188
Five-year survivals...	13	31	32	6	82
Percentage.....	92.8	70.4	40.5	11.5	43.6

Ironically enough, the majority of cervical carcinomas when seen for treatment are in the so-called "non-operable" or "far-advanced" groups, namely, Groups III and IV (Schmitz). It is to these groups that the present trend toward ultra-radical surgery—pelvic exenteration—is directed. The justification for the surgical approach in the far-advanced cases is obviously that all forms of radiation therapy have been exhausted and, therefore, such cases can only be abandoned.

Palliative irradiation has been the accepted procedure for years, with the hope that a few tumors would prove to be of a sensitive type and be entirely destroyed, and that the remainder could be held in check for various periods and the patient's discomfort be minimized. That certain cell types respond to this therapy is evidenced by five-year survival rates of 40.5 per cent and 11.5 per cent in clinical groups III and IV, respectively. In some instances pelvic exenteration has been attempted in suitable patients who have extensive disease and have not responded to irradiation therapy.

Variations in the surgical procedures are due largely to individual differences cor-

related with the extent of the local growth. Death in these patients results from complications arising in the urinary tract or gastro-intestinal tract, and the extent of the operation must, therefore, depend upon the amount of carcinomatous invasion of these structures. Hence, the operative measures utilized may be (1) *palliative*, to eliminate a severe complication in an arrested case or to restore optimum function in preparation for further treatment, or (2) *curative*, proposed in hope of cure.

*Palliative Procedures:* With invasion of the genito-urinary tract, vesical fistula formation, or ureteral obstruction with ascending infection, hydro- or pyonephrosis and resultant uremia, death intervenes. In an attempt to overcome these complications and to maintain renal function so far as possible, a transplantation of the ureters, either into the bowel or the skin, is undertaken. The decision as to the type of uretero-anastomosis, whether unilateral or bilateral, can be established only after a complete evaluation by intravenous pyelography, cystoscopy, and blood chemistry. Although ascending infection or sepsis may occur following the ureteral transplantation, the function of the kidney must be maintained to continue the chances for survival.

A similar situation arises when the carcinomatous invasion produces rectal or intestinal fistulas, with the possibility of peritoneal contamination through leakage or obstruction. Colostomy performed as a palliative measure not only affords distinct relief from the symptoms of intestinal obstruction, but will relieve the constant irritation produced by a fecal fistula. Such treatment may be beneficial both physically and mentally, enabling the patient to carry on moderate activities for a limited period of time. The inconvenience of the colostomy or the ureterostomy must be considered, but the relief of pain and the additional months of life make these inconveniences tolerable to many.

*Curative Surgical Procedures:* The justification for ultra-radical surgery as a possible curative procedure for advanced

cervical cancer is as yet undetermined. Again the extent of the disease, the amount of previous radiation therapy, and the location of the metastases form a basis upon which rests the type of operation to be employed. Under the circumstances submitted, it seems best to divide the radical surgical procedures into three groups:

1. Radical surgery indicated where the cervix appears healed but bladder invasion has been found on cystoscopy. This calls for a bilateral pelvic lymphadenectomy, hysterectomy, cystectomy, and a transplantation of the ureters into the bowel or the skin.
2. Radical surgery indicated where rectal invasion occurs with an apparently healed cervical cancer. Such procedure calls for bilateral pelvic lymphadenectomy, hysterectomy, and abdominoperineal resection of the rectum and the vagina.
3. Exenteration operation, which is the ultimate concept of ultraradical surgery, including bilateral pelvic lymphadenectomy, abdominoperineal resection of the bladder, uterus, vagina, and rectum, together with colostomy and transplantation of the ureters.

Needless to say, such procedures constitute heroic measures, involve considerable expenditure of time, and are fraught with the complications of extensive pelvic surgery. However, if the growth is so advanced that a radiotherapeutic cure is not effective and the alternative is certain death, the question of radical surgery may be presented to the doomed woman. The plan of operation in such cases cannot be executed except under the most ideal conditions. It requires (1) an anesthetist experienced in all phases of prolonged anesthesia, (2) personnel and equipment to replace the blood loss (replacement transfusions are often required) under pressure through several points of entry to combat shock, (3) a highly trained surgical staff

capable of all types of pelvic, abdominal, and genito-urinary surgery, (4) an operating room personnel well trained in this type of procedure, and (5) complete pre-operative and postoperative management by the internist to preserve the electrolyte and fluid balance.

Any radical surgery attempted without utilizing every modern facility results only in disaster. To compare the statistical results of treatment in the "abandoned" group is difficult, since the time has been too short to evaluate the number of permanently salvaged patients.

Radical pelvic exenteration is of limited application and can be attempted by few, but other surgical procedures, proved or formulated, deserve frequent consideration in the struggle against a disease that demands the utmost from all those who would enter the lists against it.

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#### SUMARIO

#### El Papel de la Cirugía en la Asistencia del Carcinoma Cervical

Tiene por objeto este trabajo considerar las indicaciones quirúrgicas en el carcinoma del cuello uterino, con mira a salvar algunos casos que de otro modo se perderían y a mejorar los resultados en estados tales como carcinoma preinvasor, carcinoma radiorresistente y carcinoma asociado al embarazo.

En el carcinoma preinvasor, comprobado por biopsias adecuadas, puede ejecutarse la panhisterectomía. Si, al hacer el examen microscópico de cortes seriados, se descubre un patrón invasor, puede entonces aplicarse irradiación complementaria.

La cirugía está igualmente indicada en casos en los que la lesión primaria no responde a la irradiación según revelan biopsias repetidas o estudios citológicos, junto con datos clínicos de fracaso en forma de infiltración progresiva o falta de regresión.

En presencia de embarazo, el tratamiento del carcinoma cervical se guía por el período de la gestación. El plan de los AA. requiere roentgenoterapia profunda para cohibir la proliferación carcinomatosa hasta alcanzar el período de viabilidad fetal. Una vez viable el feto, se aborda el parto por cesárea. A menos que el carcinoma resulte radiorresistente, los AA. no recomiendan la ejecución de la panhisterectomía al mismo tiempo que la cesárea.

La cirugía paliativa puede estar indicada en casos avanzados para facilitar alivio en presencia de invasión del aparato genitourinario o del digestivo. En presencia de enfermedad muy avanzada, sólo se emprenderá cirugía radical con mira a posible curación, si las condiciones quirúrgicas son de lo más ideales y hay a mano todos los recursos modernos.



# The Hazard of Radiation<sup>1</sup>

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THE RECENT INTRODUCTION of nuclear active materials and their rapidly expanding use in scientific and technical fields have revived and sharpened interest in the pathogenic properties of all types of short-wave-length photon energy.

While much work has been done on exposures and safe practices in the use of nuclear reactive materials, very little definite recent information exists on the danger to technicians and roentgenologic personnel from exposures to x-rays in normal diagnostic studies. Motivated by this lack of knowledge and by the new developments and renewed interest in the hazards associated with roentgenologic procedures, the Division of Industrial Health of the Michigan Department of Health made a study of the operation of fluoroscopic and roentgenographic installations in the eleven state mental hospitals, in a effort to determine whether personnel were being subjected to hazardous amounts of radiation, and if so, to devise control measures.

Mental institutions in Michigan perform practically all types of diagnostic x-ray procedures. In many cases the work is done by technicians not specially trained in roentgenology, whose main interest is in producing a diagnostic roentgenogram, with insufficient consideration for safety. Here we believed was an opportunity to find out whether or not the increasing use of x-rays for diagnostic purposes makes the cumulative dose received by roentgenological personnel significant from the health point of view. The fact that mental patients must often be held in position offered a particularly good opportunity to determine the maximum exposures encountered in diagnostic roentgenology.

A wide variety of x-ray and fluoroscopic apparatus was found in Michigan mental institutions, including machines for general and special work, machines of recent manufacture and some of very early design, with exposed x-ray tubes. Most of the machines were equipped with ray-proof apparatus, which we believe often results in a false sense of security.

## PRELIMINARY INFORMATION

When an incident beam of x-rays strikes an object, some of the rays are absorbed and some pass through, but a considerable percentage are scattered in all directions by the electrons in the atoms composing the object in the beam. The result is similar to light in a fog. Exact specifications for minimizing this scattered radiation in the most economical way are difficult to formulate because of the uncertainty of the numerous contributory conditions. The principal sources of scattered radiation in diagnostic roentgenology are: the patient, the table, the floor, and the walls. The dosage rate and quality vary widely with the size of the field, the angle of scattering, and the nature of the material. The intensity of the scattered rays depends upon the distance of the material and the dosage rate of the incident radiation. Since the contributing factors differ from one installation to another, it is impossible to formulate uniform protection data that may be used for all installations.

Radiation hazards are due to exposure to the direct beam and to the scatter. Protection against the direct beam radiation is an obvious necessity, and is achieved in the modern machines by shielding around the x-ray tube. Shielding materials may be applied most advantageously close to the

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tube. The more economical course is to purchase shielding in the form of ray-proof tubes. Only the hazard caused by the used beam passing through the aperture must then be considered.

#### NATURE OF PRESENT STUDY

The instruments used in this study were the Victoreen condenser r meter, Kelley-Koett dosimeters, and film badges. Film badges were worn for a period of one month and the number and type of all roentgenograms taken during that month were recorded. The estimated radiation exposure was calculated by multiplying the readings for each particular type of roentgenogram by the number taken during the month the badges were worn. These calculations were correlated with the film badge results. By proceeding in this manner, untenable errors in calculated results due to instrument variations were eliminated. Film badge tests have another advantage, in that they may also serve as an indication of the ray quality in parts of the film covered with different filter materials. A knowledge of the ray quality serves to indicate the origin of the stray radiation. Measurements of scattered radiation were taken under actual diagnostic conditions.

Experimental evidence sets the scattering ratio at about 1 per cent of the intensity of the main beam at a point 1 meter from the patient and at right angles to the beam. The scatter is a softer form of energy, a fact that may be used in the shield design. Below 200 kv., however, which is the range encountered in diagnostic work, the saving is not great.

In our study we were concerned mainly with the more common types of diagnostic procedure. The kilovolts, milliamperes, seconds, and beam intensities encountered for the usual roentgenographic studies were as follows:

1. Chest films: 60-70 kv., 10-15 ma., with an average direct beam intensity of 22 milliroentgens at a distance of 72 inches.

2. Skull films: 60-70 kv., 75-150 ma., with an average direct beam reading of 1.8 r at 36 inches distance.

3. Spinal films: For anteroposterior view of lumbar spine, 60-68 kv., 100-150 ma., with an average beam intensity of 3 r. For a lateral view of the lumbar spine, 72-84 kv., 192-400 ma., with an average direct beam intensity of 6 r.

4. Fluoroscopic settings: 65-78 kv., 5-15 ma., with an average examination time of about thirty seconds of machine operation. No direct beam reading was taken, since patients lying on the table absorbed a great deal of the direct beam and in varying amounts, so that measurements about them meant little in relation to beam intensity.

#### RESULTS OF STUDY

For purposes of comparison and easy reference, the results of our study are compiled in the accompanying chart. The roentgenograms taken at the hospitals over a period of a month are classified into four groups: chest, spine, skull, and miscellaneous. As used in the chart, 0 in the "Number of Exposures" column indicates that the particular type of film, though normally taken by the hospital, was not taken during the month studied. "None" indicates that the hospital did not perform that type of radiology or did not use an attendant. The duties of the attendant in the x-ray room are confined to holding the patients.

Because of the work load, some of the hospitals employed two technicians. The duties of the technicians included operation of the x-ray machine, film development, records, etc. The accompanying chart designates these technicians as "operators" and, as such, their dosage calculation was the result of the time they were operating the machine only and did not include the stray radiation that they may have received while they were performing other duties in the x-ray room. The latter, of course, would be included in the film badge exposures. It is evident that in those hospitals employing one technician the operator's dosage would be absorbed by the technician. When two technicians were employed, the operator's dosage would be split between them.

CHART I: EXPOSURE IN ONE MONTH\*  
(In milliroentgens)

Hospital	Chest			Spine			Skull			Miscellaneous		Film Badge Reading	Calculated Exposure	Calculated Attendant Exposure
	No. of Exposures	Exp. Oper.	Exp. Att.	No. of Exposures	Exp. Oper.	Exp. Att.	No. of Exposures	Exp. Oper.	Exp. Att.	No. of Exposures	Exp. Oper.			
A	61	0	854	6	0	174	32	(256)	576	36	0	50	(225)	1,604
B	46	0	425	12	60	300	0	0	0	34	0	100	64	1,680
C	56	0	1,380	36	0	1,908	0	0	0	39	0	(1,000)	0	3,666
D	152	0	1,758	16	0	None	0	0	0	75	0	25	0	912
E	101	0	1,640	16	256	None	42	56	None	161	0	250	312	1,742
F	12	0	1,742	None	None	None	None	None	None	0	0	0	0	180
G	46	0	600	2	0	None	0	0	0	36	36	0	36	600
H	140	0	700	48	0	4,800	36	0	189	136	0	100	0	7,789
I	9	0	2,800	12	48	24	None	None	None	8	12	180	60	144
J	108	0	450	18	360	18,000	8	200	2,000	46	0	140 + 100 (2,000)	280	18,600
K	200	0	6,400	9	0	90	35	0	870	59	0	200	0	8,240
			7,280						60					

\* Present maximum allowable exposure: 1,200 milliroentgens per month.

As previously stated, x-ray machines encountered in the study varied widely in age. One of the general diagnostic machines used for chest x-rays had been used for more than thirty years (in Hospital F). With this machine, in which the tube was suspended in a bell-shaped glass enclosure, open in the direction opposite to the direct beam aperture, the radiation was found to be 250 milliroentgens for five chest exposures at a distance of 5 feet. This high exposure reading was the result of improper shielding of the tube. The technician and the patient were the only persons in the room at the time the roentgenograms were taken, and the technician was adequately shielded behind a laminated lead plywood screen.

A 1922 model x-ray unit was in constant use in Hospital A for chest, skull, and spine x-rays. The operator's exposure for one anteroposterior and one lateral film of the lumbar spine was 70 mr. In conjunction with this machine, a fluoroscopic unit of about the same date of manufacture was used. In this installation it was found that the protective leaded glass back of the fluoroscopic screen had been broken and replaced with plain plate glass, resulting in a high exposure to the viewer.

In Hospital I, a portable x-ray unit was used for examinations of all types. An improperly constructed homemade fluorescent screen viewer was in use at this institution. This was held up to the eyes in a manner similar to the old stereoscope. The screen measured approximately 16 X 16 inches. The distance of the screen from the x-ray tube was determined only by the convenience of the viewer, which in most cases resulted in a direct beam exposure with a field size greater than the area of the screen itself.

With the exception of the installation at Hospital G, which was similar to that at Hospital A, the remainder of the units were of recent design. Hospital J had a recent installation, but the controls were found to be too close to the diagnostic table, with no protection for the operator except the distance factor. This lack of protection

contributed to the technician's high exposure, as can be seen from the chart.

#### DANGERS OTHER THAN RADIATION

In addition to possible radiation hazard, an electrical hazard may also be present. The voltages used to energize x-ray tubes are highly dangerous, and the best assurance of safety is the enclosure of the high-voltage parts in a shock-proof container. Most x-ray generators for diagnostic work are of shock-proof construction, but where the design is such that high-voltage conductors are exposed, operators should keep at a liberal distance from them, and should guard against the possibility of spark-over to other conductors with which a person may be in contact. The most dangerous situation is to permit the body to form a part of the high-voltage circuit, either across the tube terminals or between a high-potential lead and a low-potential lead or grounded conductor. Although high-potential circuits do not extend into the processing room, low-potential electrical outlets and fixtures may present a hazard under some circumstances. As a safeguard, the exposed portions of switches, plug outlets, lamp sockets, and the like, should be composed of insulation material. No electrical device should be touched with wet hands.

While some concern has been expressed about the ozone and oxides of nitrogen concentrations in diagnostic x-ray rooms, in only two of the oldest installations did we detect the odor of ozone. In our opinion, diagnostic machines are operated for too short a period to produce ozone and oxides of nitrogen in significant quantities.

#### SUMMARY AND RECOMMENDATIONS

1. A hazardous radiation exposure was found to exist in some of the mental hospitals of Michigan. Similar exposures may exist in many other hospitals throughout the country.

2. The most important factor in eliminating this hazard is the planned instruction of technicians in proper technics and in the dangers of radiation.

3. Outmoded and improperly designed x-ray machines constitute only one factor in x-radiation exposure of roentgenologic personnel. Other factors include the volume of roentgenograms, their type, and the technics of operation. These latter factors bear no relation to the design of the x-ray machines; high exposures may occur even with the newer types.

4. Large x-ray rooms are safer than small ones, since the amount and concentration of scatter are reduced, and the distance between the operator and the tube may be increased.

5. The proper enclosure of the x-ray tube is important.

6. The use of proper cones is important. Not only is proper coning of the beam desirable to reduce the amount of scatter and the attendant's exposure, but also to reduce the area of the patient's exposure.

7. Filtration of the beam is important. While the erythema dose for unfiltered x-rays is 300 r, for x-rays filtered through 1.0 mm. of aluminum it is 400 r.

8. Proper shielding of the operator is important.

9. The necessity for holding patients in position for x-ray work creates a definite exposure problem for attendants and technicians. A similar problem may exist in other than mental hospitals and clinics,

with unmanageable patients such as infants, small children, and individuals with senile changes.

10. Planned rotation of attendants should be carried out if patients must be held.

11. Every hospital should have several pairs of lead gloves and several lead aprons. These articles should be used.

12. It was found that simple changes often made a considerable reduction in radiation exposure. In some cases, as was shown by this study, the radiation was reduced to one-eighth of the original exposure by simply moving the controls slightly or changing the position of the technician by a few feet. Roentgenologic personnel should be conscious of these possible chances for improvement.

13. A periodic check should be made on stray radiation received by personnel. This may be accomplished by pocket ionization chambers in conjunction with film badges calibrated at about 85 kv. energy range.

14. Every effort should be made to reduce the radiation exposure to as low a figure as possible, regardless of whether or not the present exposure is below the maximum allowable limits.

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#### SUMARIO

#### El Riesgo de la Irradiación

Un estudio de las instalaciones de roentgenoscopia y roentgenografía en once manicomios del Estado (Michigan) reveló que, en algunos de ellos, los operarios y ayudantes estaban expuestos a cantidades excesivas de radiación. Aunque en algunos de los establecimientos, se encontraron aparatos anticuados y mal diseñados, esto no constituía más que un factor en la exposición del personal. Otros factores son el volumen de trabajo, la clase de radiografías (cráneo, tórax, etc.) y la técnica del examen. El elemento más importante en la eliminación de exposiciones peligrosas

consiste en el adiestramiento atinado de los técnicos en las técnicas adecuadas y los peligros que encierra la irradiación.

Observóse que la necesidad de mantener los enfermos en posición para el examen—de rigor no sólo en los manicomios sino también con enfermos reacios de otros géneros—crea un problema bien definido en lo relativo a exposición para los técnicos y sus ayudantes.

Ofrécense indicaciones para reducir al mínimo la cantidad de radiación recibida por los que trabajan en la roentgenología de diagnóstico.



## Steroids in Cancer of the Breast<sup>1</sup>

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CARCINOMA OF the breast in the female, like carcinoma of the female pelvic organs, is one of the most frequent causes of death from cancer. The U. S. Bureau of Vital Statistics gives the mortality rate as 12 per 100,000, and the yearly number of deaths from this cause is approximately 16,000.

This high death rate is a direct challenge to the medical profession, and the difference of opinion as to the treatment of choice in operable cases is evidence of the dissatisfaction with the low survival rate from the various procedures employed. Every effort to increase the salvage of these patients whether by operation, irradiation, hormone therapy, or some combination of these is worth the gravest consideration.

Bellevue Hospital (New York), the largest municipal general hospital in the country, offers an opportunity for intensive investigation and study of all types of cancer in every stage and in sufficient number to permit one to become conversant with the many phases of the disease, as well as the different methods of approach by surgical and radiation therapy.

It has long been known that ovarian sterilization has aided in the control of breast cancer, just as orchiectomy has accomplished similar effects in some males with cancer of the prostate. In view of this, an attempt was made by Farrow (15) to secure similar control effects in male and female patients with skeletal metastases from breast cancer, by the administration of estrogenic or androgenic substances. He concluded that estrogens and androgens appeared to have a similar effect on skeletal metastases from mammary cancer. Evidence was obtained that there is some growth inhibition in certain cases following withdrawal of either of these hormones and,

conversely, that an excess of either accelerates the rate of malignant growth. Farrow calls attention again to what we have often reiterated: that hormone therapy is to be employed with care in cases of carcinoma. The question of giving estrogens to post-mastectomy patients with menopausal disturbances is of importance, for one must recognize "the possibility of activating quiescent and unrecognized foci of metastatic cancer. In general, it would be much safer to forbid pregnancy or the use of estrogens in all cases of mammary cancer for at least five years, or preferably longer."

At present it is an almost universal belief that all patients with breast cancer and bone metastases who have not reached the menopause should have ovarian sterilization whether by surgery, as suggested by Horsley (18), or by irradiation, as advocated by radiologists. One cannot be certain, however, that such therapeutic procedures will affect the primary cancer growth or prevent the appearance of metastases, though clinically such effects have been observed in some cases.

Because of the effect of estrogens on cancer, we have advocated sterilization of young women with breast cancer and have carried out this procedure in every instance permitting it. Sterilization suppresses the menstrual function and related estrogenic action. Furthermore, pelvic x-ray irradiation, the method used by us, has a favorable general effect on the body and helps to heal and inhibit the formation of skeletal metastases. In substantiation of clinical observations made over a course of years, Adair *et al.* (19) report that in their experience castration materially improves results in cancer of the breast.

Whether radiation sterilization should be

<sup>1</sup> From the Radiation Therapy Department, Bellevue Hospital, Ira I. Kaplan, M.D., Director. Presented at the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 5-10, 1950.

limited to younger women with breast cancer is still a disputed question. We have treated some women past the menopause, with the idea that there may be residual estrogenic activity in the ovaries which will be suppressed only by castration.

Carcinoma of the ovary was associated with breast cancer in 8 cases in our series. What significance the ovarian cancer had in the formation of the breast cancer is not clear. We have held that the estrogenic action may be carcinogenic in its effect on the breast and for that reason have advocated sterilization. With cancer already in the ovary, what is the effect on breast cancer? Judging from our cases, this question is still unanswered.

The recent literature has contained many reports concerning the use of steroids in the treatment of metastatic breast carcinoma. Before any attempt can be made to evaluate the usefulness of hormone treatment, one must review the duration of life after discovery of the cancer. Wade (20), in a study of 27 patients, found eight months to be the average duration of life in untreated cases after the discovery of metastases, and in no case was there evidence of spontaneous regression or resolution of the disease. She also stated that she had found no apparent relationship between the length of life and the histologic degree of malignancy. She further cited Greenwood's series of 651 cases, in which the duration of life without treatment was 38.3 months from the onset of the first symptoms. Daland, also quoted by Wade, failed to observe any instance of spontaneous regression in his series of 100 cases of untreated breast carcinoma. He found that the average duration of life from the time of onset of the first symptom was 40.5 months; 22 per cent lived five years without any treatment, and 5 per cent lived ten years without any treatment.

According to the Council of Pharmacy and Chemistry of the American Medical Association (2), "surgical treatment and irradiation, singly or in combination, still must be considered the primary forms of treatment, steroid hormone therapy being

reserved only for those cases in which orthodox methods either cannot be applied or have proved unsuccessful." Other investigators have substantiated this view.

Herrmann, Adair, and Woodard (7) stated that estrogens exert a favorable result predominantly in women above sixty years of age. Nathanson (11) also reported that favorable responses to estrogens are confined to older women. He further expressed the view that osseous metastases seldom show a favorable response to estrogenic therapy, though both the primary tumor and soft-tissue metastases may be benefited, the response of the primary tumor, however, being only temporary. The Council on Pharmacy and Chemistry (3) has further clarified the issue in stating that any patient who is still menstruating or has menstruated within one year should not receive estrogens, as the rate of growth of the malignant process may be accelerated.

Castration, by x-ray or surgery, has produced a favorable effect on osseous metastases. Following induction of an artificial menopause by ovarian irradiation, Farrow and Woodard (5) found a temporary retardation of skeletal metastases, which after several months to two years showed evidence of reactivation. In our cases testosterone has been employed after castration has had its effect.

While the androgen has been used here primarily in the treatment of bone metastases, it has also been employed for patients who have failed—or ceased—to show a favorable response to estrogen. Other investigators have also advised adherence to this principle.

The response to hormonal therapy has been divided into subjective and objective. Van Winkle (2, 3) has defined subjective response not merely as an increased sense of "well-being," but as including marked relief of pain and/or a lessening of the complaints referable to the disease. Objective response has been defined as recalcification of bony lesions, demonstrated roentgenographically, or regression of soft-tissue lesions. It has been stated that the dura-

tion of therapy influences objective improvement, and that osseous lesions usually show more rapid response than soft-tissue lesions.

In our own series of 50 patients treated, 51.7 per cent showed subjective improvement, and 24.1 per cent showed objective improvement. Those who showed subjective improvement were treated with estrogens, and of these 2 showed objective signs of improvement also. The time of improvement varied from three to four weeks, and lasted two years in one case with repeated series. Of the 50 women treated with androgens, 3 were "overlap" cases—i. e., treated also with estrogens—finally failing to show response to either steroid after objective response in 2 previous series.

The response to steroid therapy in this present series is in no way a true picture of what it should be. During the early days, patients were admitted for hormonal therapy only when practically moribund. Thus the percentage of objective response has undoubtedly been low, as compared to what it would be in a larger group.

The majority of patients in this series received testosterone propionate, 100 mg. three times a week. Three were given 25 mg. three times a week. One of these showed an acceleration of metastases, later controlled with 100 mg. three times a week. The largest total dose of testosterone in any single series of injections was 7,000 mg., and the largest total dose to any patient 16,300 mg.

The hormones have been given in a series of continuous injections and then discontinued until evidence of improvement ceased or extension of the malignant process occurred. The progress of these patients was followed closely by skeletal roentgenograms, and actual comparative measurements were made wherever possible in soft-tissue lesions.

In those patients treated with testosterone, hirsutism and voice change were frequent.

Alkaline phosphatase values were initially elevated in 27 of the series, and in 14

of these there was a drop to normal during and subsequent to hormone therapy. The figure remained high in the other 13 and became elevated in 12 additional patients (total 52 per cent) during and following therapy. The elevation ranged from 4.4 to 12.7 Bodansky units. A level of 25 to 50 units has been reported as suggestive of liver damage or liver metastases.

Hypercalcemia, a more serious complication, was treated by intravenous infusions of 2.5 per cent sodium citrate solution and discontinuance of the testosterone therapy. Testosterone has caused a decreased renal excretion of potassium, inorganic phosphorus, total nitrogen, and sodium. Thus, patients with cardiac disease required supplemental therapy, such as decreased salt intake, and diuretics to diminish fluid retention.

Pathologic fractures of the extremities occurred in 6 of our patients. Concurrent x-ray therapy was given to these fracture areas with complete healing in only 3 instances. Compression fractures of the vertebrae were noted in 28 patients. The striking features of the latter were the lack of neurological symptoms and the mildness of the pain in spite of extensive involvement and frequent collapse of the vertebrae. The weakened, involved bones have made all the more necessary frequent adequate examination of the skeletal system, especially the weight-bearing areas, so that supportive measures, such as braces and radiation therapy, could be administered prophylactically.

It has been difficult to assess the actual relief obtained. In several instances, however, patients completely bedridden have become symptom-free and ambulatory. On the basis of this observation, we combined steroids with radiation therapy, particularly in the presence of metastases in the long bones or weight-bearing areas.

This study has not yet been in progress long enough to determine if there has been any change in longevity, although 20 of the patients were still alive at the time of writing. The majority that have died did not show a favorable response to the initial

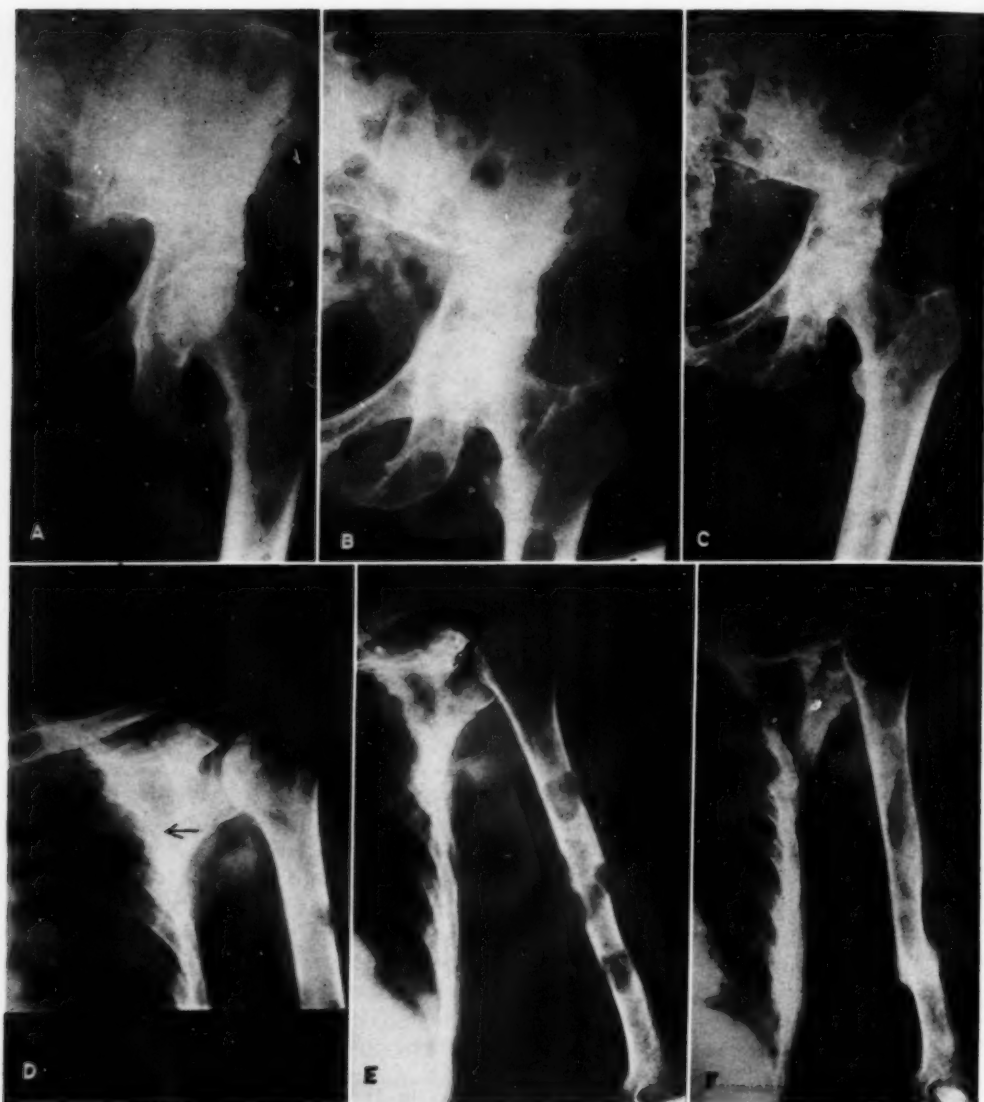


Fig. 1. Case I

- A. Aug. 10, 1949. Numerous osteolytic metastatic areas in left half of pelvis and upper third of left femur.  
 B. Sept. 14, 1949. Marked increase in number and size of osteolytic areas as compared with film of one month earlier (A).  
 C. Nov. 28, 1949. Only slight continued increase in number and size of metastases since September (B).  
 D. Aug. 10, 1949. Film of left shoulder showing numerous osteolytic metastatic areas in scapula, ribs, and humerus.  
 E. Sept. 12, 1949. Increase in number and size of osteolytic areas, with a pathological fracture at the junction of the middle and distal thirds of the left humerus.  
 F. March 22, 1950. Recalcification of osteolytic areas in scapula, ribs, and humerus. The pathological fracture is completely healed, with abundant callus formation.

course of steroid therapy. It has been our impression, however, that steroids have increased the length of life in those persons

who demonstrated a definite objective response to combined steroid and x-ray therapy. In no instance was the disease





Fig. 2. Case II

- A. July 29, 1949. Right half of pelvis, showing osteolytic metastatic areas in ischium and acetabulum.  
 B. Right half of pelvis three months later, showing beginning recalcification of metastatic areas.  
 C. March 1, 1950. Marked recalcification of metastatic areas in acetabulum and ischium as compared with earlier films.

cured by the administration of steroids alone.

The following cases are illustrative:

**CASE I:** A. C., a 73-year-old female, first noticed a small lump in the left breast, in the inner lower quadrant adjacent to the nipple, in June 1948. Three days later a left radical mastectomy was performed for adenocarcinoma, but no positive nodes were reported in the axilla. The patient remained well until June 1949, when she experienced chest pain on respiration. The pain continued, and on Aug. 3, 1949, a node was found in the left axilla, which proved microscopically to be metastatic breast carcinoma. Laboratory studies on Aug. 9 showed phosphorus 3.4 mg. per cent, calcium 13.3 mg. per cent, alkaline phosphatase 2.4 Bodansky units.

A roentgen survey on Aug. 10 revealed generalized osteolytic metastatic involvement of the skull, spine, pelvis, ribs, scapulae, humeri, and femora (Fig. 1, A and D). On Aug. 17, testosterone therapy was instituted, 25 mg. three times a week, and analgesics were given for the pain. The patient experienced increase in appetite and well-being, but on Sept. 12 showed swelling, pain, and deformity of the distal third of the left humerus, where a pathological fracture was found (Fig. 1E). The arm was immobilized and irradiated, and the dosage of testosterone was increased to 100 mg. three times a week. Two days later the blood calcium had risen to the dangerous level of 15 mg. per cent and the alkaline phosphatase had dropped to 1.6 Bodansky units; phosphorus was 1.9 per

cent. The blood count remained normal, except for a slight leukocytosis of 9,500.

Under the new regime the patient showed definite improvement, with healing of the pathological fracture, and gradual decrease of pain. The blood calcium dropped to 10.0 mg. (Oct. 14) and the alkaline phosphatase rose to 6.8 Bodansky units. Films taken on Nov. 28, however, showed a continued increase in the size and number of osteolytic areas in spite of the generally improved condition. Figure 1C shows the extensive process in the pelvis. Testosterone was discontinued Jan. 14, 1950, after 7,000 mg. had been given. Films obtained on Jan. 25 showed some recalcification for the first time, though the patient had been without analgesics for several months. Examination on March 22 found the patient comparatively well, with some side-effects from the testosterone, namely, hirsutism, slight balding of the scalp, and hoarseness. Films at that time showed further recalcification of the left humerus (Fig. 1F) but only slight recalcification of the pelvic bony metastases. The last film (April 14) revealed further recalcification, but the cranial vault was riddled with metastases. There were definite signs of cerebral involvement. Death occurred April 26, 1950.

**CASE II:** A. G., a 52-year-old married white female had a right radical mastectomy in 1946, without postoperative irradiation. She had begun to experience pain in the lower back and thighs four months before she was seen by us on July 21, 1949.

There was a history of buttock injections with heavy metals for syphilis many years earlier.



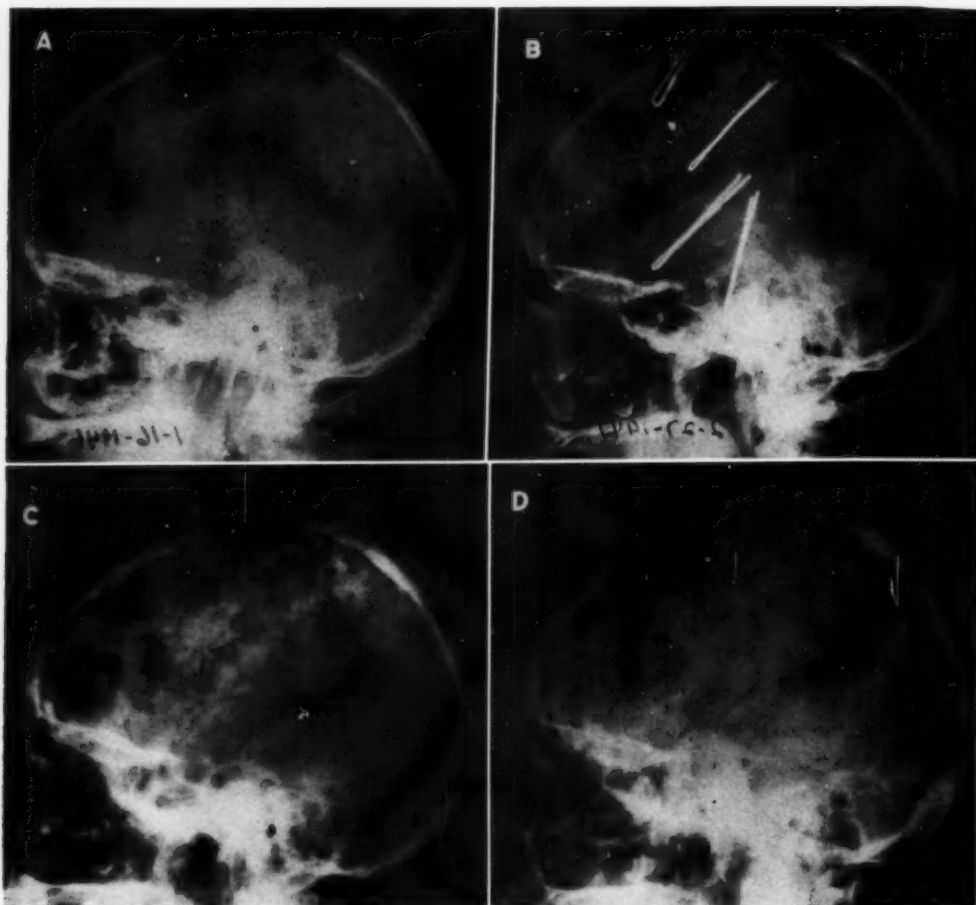


Fig. 3. Case III

- A. Jan. 16, 1946. Right lateral view of skull showing numerous osteolytic metastatic areas.  
 B. Feb. 27, 1947. Some recalcification of metastatic areas observed thirteen months earlier. (Bobby pins are artefacts.)  
 C. Aug. 24, 1949. Reactivation of metastatic lesions with increase in number and size, two and a half years later.  
 D. March 15, 1950. Beginning recalcification of metastatic lesions for the second time, seven months after film shown in C.

Physical examination showed a well healed right radical mastectomy scar and pain to pressure over both ischial tuberosities, radiating down the inner aspect of either thigh to the knee. The patient was unable to walk without support, because of the pain. Roentgenograms taken on July 29 (Fig. 2A) showed osteolytic metastases in both ischia and in the right acetabulum. The laboratory findings were as follows: non-protein nitrogen 30 mg. per cent; Wassermann reaction negative; phosphorus 3.63 mg. per cent; alkaline phosphatase 4.6 Bodansky units.

On July 29, the patient began receiving testosterone propionate, 100 mg. three times a week.

In three weeks there was marked relief of pain, so that the patient no longer needed analgesics. In eight weeks she was able to return to her factory job, working eight hours a day.

In three months there was definite evidence of beginning recalcification of the pelvic osteolytic metastases (Fig. 2B), and the blood chemistry showed a rise in the alkaline phosphatase to 5.0 Bodansky units.

During this time the patient noticed moderate hirsutism, voice deepening, and slightly increased libido. The testosterone was discontinued Jan. 20, 1950, after a total dose of 6,000 mg. had been given. This patient has now continued in a state

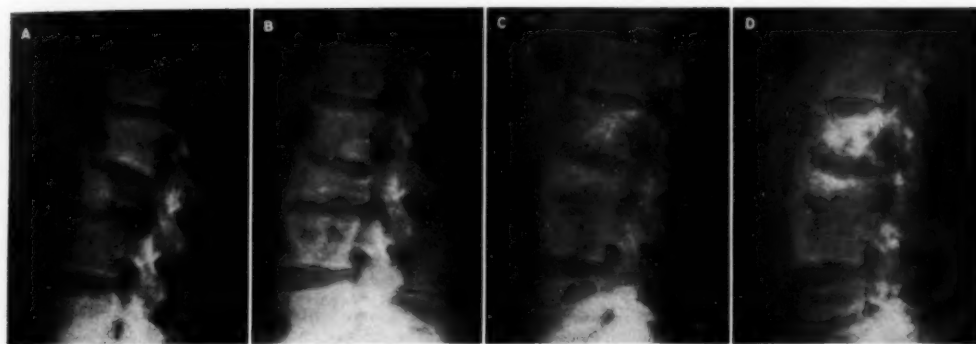


Fig. 4. Case III

- A. Jan. 16, 1946. Marked osteolytic processes in lumbar vertebrae.  
 B. Feb. 27, 1947. Recalcification of metastatic processes thirteen months later.  
 C. Aug. 24, 1949. Reactivation of metastatic process after two and a half years, with new lesions demonstrable.  
 D. March 15, 1950. Beginning recalcification in lumbar spine seven months later.

of well-being for nine and a half months, and pelvic films of March 1, 1950 (Fig. 2C) and Sept. 15, 1950 showed progressive recalcification of the pelvic metastases.

CASE III: E. H., a 57-year-old white female, first noticed a retraction of the skin over the upper medial quadrant of the left breast in 1934. On Aug. 12, 1937, after preoperative roentgen therapy had been administered to the left breast, a left radical mastectomy was performed. This was followed by postoperative irradiation to the left chest wall and axilla. The patient was comparatively well until June 1943, when lumbosacral metastases developed, and were treated with x-ray therapy. From October to December 1945 the patient received x-ray therapy to the dorsal spine and pelvis, as well as testosterone, 100 mg. three times a week, for a total dose of 1,400 mg. Improvement followed until 1946 (Figs. 3A and 4A) when x-ray therapy was again given to the pelvis, with a similar course of testosterone, a total dose of 1,400 mg.

After each series of treatments there were some recalcification of the bone lesions and general relief of symptoms. Films taken in February 1947 (Figs. 3B and 4B) still showed recalcification of the lesions in the dorsal and lumbar spine, but a mixture of osteoplastic and osteolytic reaction in the non-irradiated skull. Since that time the patient has received three more series of injections of testosterone propionate, followed each time by relief of symptoms and reversal of the osteolytic reaction. The total dose for all series of injections to date has been 10,500 mg., the last series having been completed Nov. 8, 1949.

Skeletal films of Aug. 24, 1949 (Fig. 3C and 4C), compared with the latest, taken March 15, 1950 (Figs. 3D and 4D), again showed a slight beginning recalcification of the metastatic lesions. The

patient was well when last seen in the clinic on Oct. 20, 1951.

#### CONCLUSIONS

1. Subjective improvement was observed in 51.7 per cent of a series of 50 patients with advanced breast carcinoma receiving steroids, whereas objective improvement was demonstrated in only 24.1 per cent.

2. Evidence of repeated objective improvement was observed with additional courses of steroids.

3. The relief of symptoms has made this form of treatment of definite therapeutic value in the patients who showed a favorable response.

4. Testosterone propionate has been of maximum value when administered in large doses, 100 mg. three times a week.

5. X-ray therapy, especially to weight-bearing areas, in combination with testosterone has given maximum relief in most cases.

6. Sterilization in young women with breast cancer is definitely advocated.

7. The patients treated with steroids alone have not been followed for a sufficient length of time to permit of any definite conclusion as to actual change in longevity in the presence of far advanced metastases. However, it is believed that the length of life has been increased in those patients who show a favorable steroid response.

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## SUMARIO

## Los Esteroides en el Cáncer de la Mama

Las hormonas esteroideas han sido utilizadas por los AA. en las enfermas con carcinoma mamario. Los andrógenos han sido usados primordialmente para las metástasis óseas, pero también en las enfermas que no respondieron—o dejaron de responder—favorablemente a los estrógenos.

De 50 enfermas tratadas, 51.7 por ciento mejoraron subjetivamente, en tanto que 24.1 por ciento revelaron mejoría objetiva en forma de recalcificación, observada radiográficamente, de lesiones óseas o regresión de metástasis en tejidos blandos.

La mayoría de las pacientes recibieron propionato de testosterona, 100 mg. tres veces por semana. El tratamiento fué administrado en una serie de inyecciones continuas y luego suspendido hasta que cesaban los signos de mejoría o había difusión

del proceso maligno. La dosis total máxima en una serie de inyecciones fué de 7,000 mg. y el total máximo para una enferma dada de 16,300 mg.

En algunos casos, una combinación de roentgenoterapia, aplicada en particular a las zonas que sobrellevan el peso, y de inyecciones de testosterona proporcionó el mayor alivio.

Aunque es demasiado pronto para sacar conclusiones relativas al efecto de los esteroides sobre la duración de la vida en el cáncer mamario, la impresión formada es que se ha prolongado la vida en las enfermas que respondieron favorablemente al tratamiento. De las pacientes de esta serie que fallecieron, la mayoría no reveló respuesta favorable a la tanda inicial de esteroides.

## Further Studies on the Radiosensitivity of the Analogous Mouse Mammary Tumors dbrB and C3H,

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THE PURPOSE OF this communication is to present a survey of findings from an extensive series of experiments on the radiobiological characteristics of two analogous mouse mammary tumors. An attempt will be made to interpret several interesting phenomena which were brought to light during the course of this research, and finally, a discussion will be presented of a possible technic for radiation therapy which arises logically from a consideration of these and previous results.

The presentation is in three parts which correspond to the three phases which have evolved from this work:

- Part I. Quantitative Analysis of the Growth Rates of dbrB and C3H Tumors Before and After Irradiation.
- Part II. Intermediary Metabolism of the Control and Irradiated Tumors.
- Part III. Feasibility of Applying Large Doses of Roentgen Radiation by the Use of Small Areas.

For the sake of clarity a concise summary of previous findings and background will first be given.

The mammary tumor of the dba strain of mice, designated the dbrB tumor, diagnosed as an adenocarcinoma, has a latent period<sup>2</sup> of about four to six days and results in the death of the host within three weeks. The mammary tumor of the C3H strain of mice, referred to as the C3H tumor, and also diagnosed as an adeno-

carcinoma, has a latent period of about sixteen to eighteen days and kills the host within three months.

A dose of about 5,000 r was required to prevent the growth of implants of the dbrB tumor, approximately  $2 \times 2$  mm., in hosts of the dba strain, whereas, a dose of about 2,800 r was necessary to prevent growth of implants of the C3H tumor, of about the same size, in hosts of the same strain (1). For explants in tissue culture of the dbrB tumor, also about  $2 \times 2$  mm. in size, a dose of about 80,000 r was required to prevent growth *in vitro*, while for the C3H tumor a dose of about 130,000 r was necessary to produce the same effect on explants of similar size (2). That a larger dose of radiation is needed to prevent cellular growth *in vitro* than *in vivo* has been noted by several investigators, as well as by the writer (3-7).

An observation of particular interest was that in the *in vivo* experiments, using implants, the C3H tumor was more radiosensitive than the dbrB tumor, while in the *in vitro* experiments, using explants, the dbrB tumor was the more radiosensitive.

Results obtained from further studies on the actively growing tumors treated with x-radiation *in vivo* correlate with those obtained on irradiated implants. It was found that doses ranging from 16,000 to 24,000 r were required to produce total regression of well developed dbrB tumors (1.0-1.5 cm.), while for the C3H tumor, doses ranging from 8,000 to 12,000 r were sufficient to produce the same effect (8).

The concept that faster growing, anaplas-

<sup>1</sup> From the Cancer Research Laboratory, Department of Hospitals, City of New York, and the Department of Biology, Graduate School of Arts and Science, New York University. Presented at the Thirty-sixth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 10-15, 1950. Some data also presented at the International Congress of Radiology, London, July 1950.

This investigation was supported by grants from the National Cancer Institute, U. S. Public Health Service, and from the Damon Runyon Fund.

<sup>2</sup> Latent period is defined here as the time elapsing between implantation of a tumor graft and the appearance of a measurable tumor.



tic tumors are more radiosensitive than slower growing ones is in accord with results of the *in vitro* experiments, in which the faster growing dbrB was found to be more radiosensitive, but is not in accord with results of the *in vivo* experiments. The question arose as to why a tumor should be relatively more radiosensitive when grown *in vitro* than *in vivo*.

To throw light on this problem experiments were carried out on the metabolism of these tumors *in vitro*. It was shown, by the use of the Barcroft-Warburg manometric technic, that the oxygen uptake and aerobic glycolysis of the dbrB tumor were about three times greater than in the C3H tumor (9). Based on the higher over-all metabolic activity, *in vitro*, of the dbrB tumor, the tentative explanation was offered that a faster and greater recovery following irradiation might take place in this tumor when grown *in vivo*, due to the faster turnover of metabolites. In this way, the toxic substances produced by irradiation may be "carried away" and a greater recovery of partially injured cells may then take place. The greater vascularity and secretory activity of the dbrB tumor enhances the turnover of metabolites. To gain more evidence in regard to this hypothesis and to throw light on the inherent biological and physiological characteristics of these tumors, detailed studies were carried out on the mitotic indices and on the intermediary metabolism of control and irradiated dbrB and C3H tumors, the results of which will be presented.

#### I. QUANTITATIVE ANALYSIS OF THE GROWTH RATES OF dbrB AND C3H TUMORS BEFORE AND AFTER IRRADIATION

The rates of growth of dbrB and C3H tumors were originally determined by external measurements of two or three dimensions with calipers, and were found to be in a ratio of about 3:1 (8). The question arose whether the significant increase in the size of the faster growing tumor (dbrB) could be accounted for by a quantitative difference in the mitotic activity or by other factors.

To throw light on this question, a procedure was required which would determine the growth activity of tumors on a more quantitative biological basis than external measurements alone. Moreover, in studying the effects of radiation there is a need for a practical method of evaluating quantitatively the effects of a given dose on the growth activity of a tissue. This is particularly true in therapy of malignant tumors.

Studies *in vitro* with tissue-culture technic and *in vivo* by the use of biopsy material have shown that not all cells are destroyed outright except with tremendous radiation doses. Such large doses cannot be applied, in one exposure, to tumors *in vivo* because of the damaging effects on surrounding normal tissues, particularly the skin. Consequently, in radiation therapy the total dose required for tumor destruction must be fractionated and applied over given periods of time. In employing such fractionated treatments, one faces the problem of permitting the uninjured tumor cells to continue growing and the partially injured cells to recover before a subsequent radiation dose is given. It is of importance, therefore, to ascertain the extent of damage done to the tumor tissue and the extent of its recovery following each dose of radiation in order to adjust the over-all time within which the course of treatment should be carried out. Thus, a practical procedure permitting a quantitative evaluation of growth potentialities of tumors before and during treatment would be of great value.

Chalkley's method (10), which was devised for quantitative evaluation of spatial distribution of morphologic tissue components, was found useful in this respect. This method has been applied in studying the quantitative relationships of various tissue components by a number of investigators (11-14) and has been adapted by the writer for the determination of growth rates of tumors. The first results obtained were recently reported (15). Additional observations and a brief description of the method will be presented here.



### Experimental

Well developed, actively growing tumors (dbrB and C3H) about 1.0 to 1.5 cm. in diameter, growing in hosts of the dba and C3H strains of mice, respectively, were used in this study. For radiation purposes, the device described by the writer (8), which permits the exposure of the tumor while the rest of the animal is protected,

solution. It is deemed essential, for purposes of pre- and post-irradiation comparison, to analyze portions from the edges of the tumors, since the central portions both of the treated and untreated tumors are usually more or less necrotic.

Paraffin sections 4 micra in thickness were stained with hematoxylin and eosin, and by Feulgen's procedure. The latter

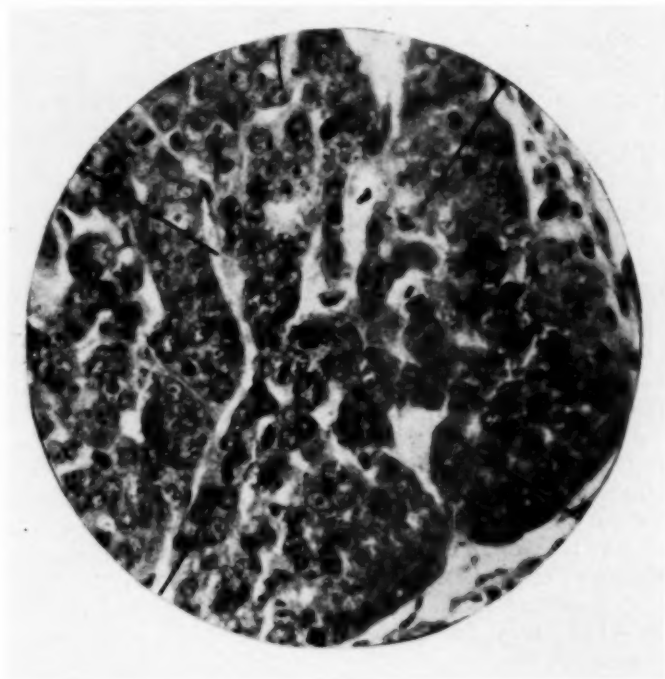


Fig. 1. Microscopic field showing arrangement of pointers. The shortest pointer, at the top of the field, serves as an index and is placed on a resting cell. The reading is: 1 mitotic cell; 1 resting cell; 1 disintegrating cell; 1 empty space.  $\times 400$

was employed. The physical factors used were: 200 kv., 20 ma., 0.5 mm. Cu plus 1.0 mm. Al filtration, h.v.l. = 1.1 mm. Cu, F.S.D. 12.5 cm., average intensity 602 r/min.  $\pm 5$  per cent.

The animals were killed by cervical dislocation and the irradiated tumors were excised within various intervals following irradiation. Due to regional variations in the growth potentialities of tumors, several sections from various parts of the edges of the tumors, control and irradiated, were removed and immediately fixed in Zenker's

method permits a more specific identification of cells in active division.

Microscopic fields containing the most intact portions of the tumor were chosen at random for analysis. Figure 1 illustrates a typical field and the arrangement of the pointers. The latter can be made by gluing very fine wire or eyelashes to the eyepiece diaphragm. The shortest pointer is focused on a selected object; here, on an intact nucleus. The objects directly beneath the tips of the other four pointers are recorded. In essence, this method permits

TABLE I: VOLUME RATIOS OF MITOTIC TO RESTING CELLS OF dBrB TUMORS

Number of Mouse	Age of Tumor	Mitotic Index*
I	5 days	1:43.8
II	10 days	1:53.8
III	10 days	1:50.0
IV	13 days	1:53.8
V	15 days	1:46.7
Average of 5 tumors		1:49.6

\* Ratio of dividing to resting cells in an extended volume of tissue.

TABLE II: VOLUME RATIOS OF MITOTIC TO RESTING CELLS OF C3H TUMORS

Number of Mouse	Age of Tumor	Mitotic Index*
I	10 days	1:87.5
II	14 days	1:63.6
III	41 days	1:77.7
IV	41 days	1:63.6
V	57 days	1:70.0
Average of 5 tumors		1:72.5

\* Ratio of dividing to resting cells in an extended volume of tissue.

the determination of volume ratios of various tissue components. Since fields are taken at random, one can obtain a reasonable estimation of the make-up of the whole tissue. For further details of the method, reference is made to Chalkley's original publication (10).

Due to the inhomogeneity of tumor tissue, it was at first intended to take several factors as criteria of the effectiveness of given doses of radiation, such as the number of resting cells in relation to cells in active division, to disintegrated cells, to hemorrhagic areas, etc. Preliminary analyses, however, showed that such a variety of observations made the results too complex. The most reproducible ratios obtained were those of mitotic to resting tumor cells. Consequently, it was decided to take these ratios as the basis for evaluating the proliferative capacity of both control and irradiated tumors. Further, it was deemed of more significance to know the relative number of viable cells present than of destroyed cells. In no case were doubtful or abnormally dividing cells included in the ratios. This simplifies the analysis and makes a comparison of results obtained from control and irradiated tumors more reliable, since abnormal mitoses are present in variable numbers in non-irradiated tumors.

The number of mitotic cells hit during the counting of 700 hits on resting tumor cells within the intact portions of the tumor section formed the basis for the ratios. Chalkley demonstrated that stabilizing ratios can be obtained from 500 hits. For the sake of even greater precision, counts based on 700 hits were used in this

investigation. The ratio for each tumor section so analyzed was obtained by dividing the 700 hits on resting cells by the number of hits on mitotic figures.<sup>3</sup>

### Results

Counts made on five actively growing dBrB and five C3H tumors are recorded in Tables I and II, respectively.

The volume ratios of mitotic to resting tumor cells of the dBrB tumor range from 1:43.8 to 1:53.8, the average being 1:49.6. The age of the tumor, *i.e.*, the time elapsing between implantation of tumor fragments and the removal of the tumor for histologic analysis, varied from five to fifteen days. This period is the time during which the tumor increases in size most rapidly. The average size attained by the five tumors within this period was  $23 \times 15 \times 10$  mm. The relatively small variation of the volume ratios of mitotic figures to resting cells of these five tumors during their most active period of proliferation seems to indicate that mitotic activity does not entirely account for the rapid increase in tumor size. The presence of cystic empty spaces, as seen in microscopic sections, offers a possible explanation for the sudden increase in size which is not to be accounted for by mitotic activity alone. Engorgement of the glandular structures with amorphous material in their lumina, and

<sup>3</sup> The following definitions are used throughout this paper:

*Mitotic cell:* Any cell in active division, from the earliest recognizable prophase to the separation of daughter cells.

*Resting cell:* Includes those cells which are not in active division.

*Hit:* The coincidence of the tip of the pointer with the cell.

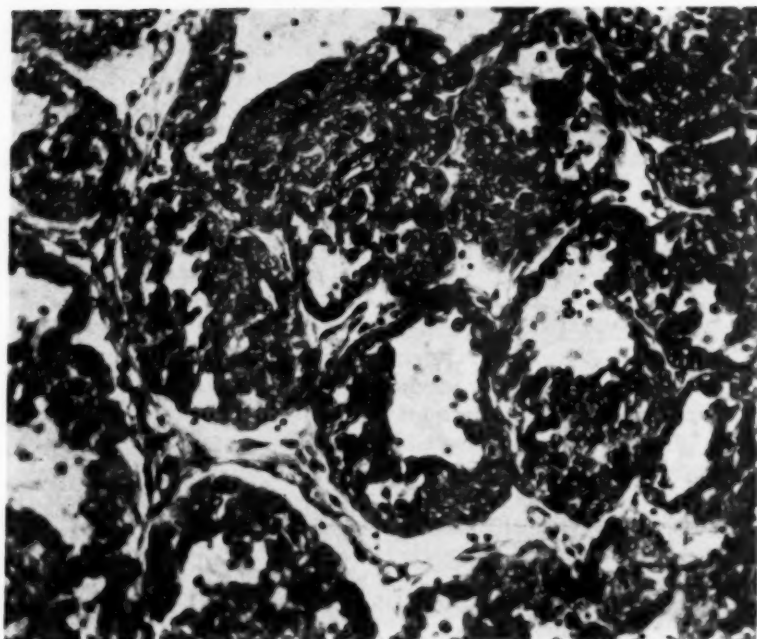


Fig. 2. Section of the dbrB tumor. Note dilatation of the lumina of the acinous structures, some of which contain secretory material; also, the empty spaces.  $\times 250$ .

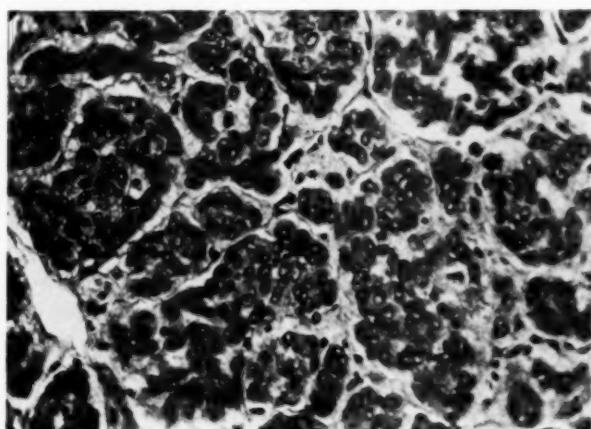


Fig. 3. Section of C3H tumor, showing densely arranged acinous structures separated by fibrous connective-tissue stroma.  $\times 250$ .

empty spaces, indicating the secretory activity of the dbrB tumor, support this view (Fig. 2).

In the C3H tumor (Table II) the ratios average 1 mitotic to 72.5 resting cells, ranging from 1:63.6 to 1:87.5. Since the C3H tumor grows more slowly, the ages of

the tumors are considerably greater than those of the dbrB tumors. The greatest increase in size occurs within three or four weeks following implantation, at the end of which time the tumors average about  $9 \times 7 \times 6$  mm. From the ratios of mitotic to resting cells, it appears that this tumor

TABLE III: VOLUME RATIOS OF MITOTIC TO RESTING CELLS OF dbrB TUMORS FOLLOWING IRRADIATION

Number of Mouse	Dose of Radiation	Post-Irradiation Time	Mitotic Index*
I	5,000 r	1 hour	1:350
II	5,000 r	24 hours	1:41.0
III	5,000 r	13 days	1:87.5
IV	10,000 r	7 days	1:87.5
V	10,000 r	26 days	1:100
VI	12,000 r	1 hour	1:700
VII	12,000 r	50 hours	1:89.6
VIII	16,000 r	22 hours	1:350
IX	16,000 r	6 days	1:700

\* Ratio of dividing to resting cells in an extended volume of tissue.

has a rather even growth activity within the three weeks following the latent period. The histologic structure (Fig. 3) is rather compact in contrast to that of the dbrB tumor (Fig. 2). (The significance of the differences in their physiological make-up as regards radiosensitivity will be brought out in the discussion.)

The reproducible counts made by several individuals and the relatively narrow range of the results obtained from the control tumors justifies the use of this small number as a basis for comparison with irradiated tumors.

In the irradiated tumors, as in the controls, only the most intact areas were analyzed. From a previous study (8) it is known that well developed, actively growing dbrB tumors require doses ranging from 16,000 to 24,000 r, and C3H tumors doses from 8,000 to 12,000 r, for total destruction, depending upon the size of the tumor. By taking as a criterion the greatest number of mitoses which could be found in a microscopic field, it was noted that a greater recovery occurred in the faster growing dbrB tumor. To gain additional information on this point, Chalkley's method was applied to dbrB tumors which had received 5,000 to 16,000 r and to C3H tumors receiving 2,000 to 12,000 r.

It should be emphasized that the main interest in this analysis was to find the quantitative relationship between the resting and mitotic cells in the intact portions of the tumors. Accordingly, only those sections which showed mitotic activity were analyzed and no consideration was

given here to the cytological changes and degree of degeneration which occurred in other portions of the tumor. Some of these characteristic changes were described in previous publications (8, 16) and more data on this subject will be presented in a forthcoming paper.

Analysis of some typical results (Table III) reveals that one hour after a dose of 5,000 r the mitotic index was 1:350. The same dose yielded a ratio of 1:41.0 twenty-four hours after irradiation, and a ratio of 1:87.5 thirteen days post-irradiation.

TABLE IV: VOLUME RATIOS OF MITOTIC TO RESTING CELLS OF C3H TUMORS FOLLOWING IRRADIATION

Number of Mouse	Dose of Radiation	Post-Irradiation Time	Mitotic Index*
I	3,000 r	24 hours	1:233
II	4,000 r	2 days	1:116
III	6,000 r	13 days	1:63.6
IV	12,000 r	9 days	1:700

\* Ratio of dividing to resting cells in an extended volume of tissue.

On comparison of the above data with the average mitotic index of non-irradiated dbrB tumors (1:49.6), it appears that a significant decrease in mitotic activity occurred one hour after exposure, but after twenty-four hours the mitotic index approached that of the non-irradiated tumor. The reduction of growth activity on the thirteenth day indicates a delayed effect.

A mitotic index of 1:87.5 was found in dbrB tumors seven days following exposure to 10,000 r, and of 1:100 twenty-six days after such exposure.

The mitotic index of irradiated dbrB tumors one hour after exposure to 12,000 r was 1:700, and fifty hours after applying this dose the index was 1:89.6. These findings indicate an immediate reduction in the mitotic activity, followed by a rapid increase at fifty hours.

The mitotic index of dbrB tumors twenty-two hours following exposure to 16,000 r was 1:350, while six days after exposure it was 1:700, indicating a progressive decrease in the growth potentiality of the tumor with the increase of the dose.

In Table IV are recorded results obtained



from analyses of four irradiated C3H tumors. Although this number is too small to permit conclusions, the fact that the results are in correlation with previous observations made on this tumor (8) justifies their presentation here.

A mitotic index of 1:233 was obtained twenty-four hours after exposure to a dose of 3,000 r, indicating a sudden drop in mitotic activity (average index of non-irradiated C3H tumors, 1:72.5). Two days following a dose of 4,000 r the mitotic index was 1:116, indicating that growth activity continued, but at a slower rate. Experiment 3 (Table IV), which yielded a mitotic index of 1:63.6 thirteen days following exposure to 6,000 r, indicates that in the intact portions of the tumor the growth activity resembles that of a non-irradiated tumor.

Exposure of a C3H tumor to 12,000 r resulted in a mitotic index of 1:700 nine days following treatment.

It is of interest that indices of 1:700 were obtained in both tumors (dbrB and C3H) when they were exposed to threshold doses of irradiation. It would seem that an index of this order of magnitude might serve as an indication of the threshold dose for the given tumor. Much more work must be done, however, before such a conclusion can be drawn.

#### Discussion

It should be recalled that the purpose of this investigation was to bring forth additional information regarding the relative biological characteristics of the two analogous mouse mammary adenocarcinomas, dbrB and C3H.

Since mitotic indices of the dbrB and C3H tumors were found to be 1:49.6 and 1:72.5, respectively, and the growth of implanted tumor tissue is in a ratio of 3:1, it follows that the relatively great increase in size of the dbrB tumor is not due to the mitotic activity alone, but may be partly explained by its inherent secretory tendency, which is evidenced by engorgement of the glandular lumina and the presence of cystic spaces, as seen in microscopic sec-

tions. Such a biological characteristic must be taken into consideration in evaluating growth activity of a tumor when gross measurements are used.

It was of particular interest that, following sublethal doses of x-rays, the dbrB tumor showed an earlier and more pronounced return of mitotic activity than the C3H tumor. This observation substantiates a previous study (8) in which the greatest number of mitotic figures that could be found in a microscopic field of the section was taken as a criterion. The greater prevalence of mitotic activity in the dbrB tumor may be explained as follows. A higher proportion of incipient dividing cells is available in the dbrB tumor than in the C3H tumor; if these are not sufficiently affected by radiation, they may reach a stage of division soon after exposure. Further, the higher metabolic rate of the dbrB tumor (9) may enhance its recovery. This phase of the problem will be further discussed in the second part of this presentation.

Glücksman and Spear (17) and Lasnitzki (18) evaluated the response of tumors to irradiation on a quantitative basis. These investigators analyzed tumor sections by counting 300 to 500 cells, in given microscopic fields, taking into account resting cells, cells in division, keratinizing cells, and degenerated cells. In essence, such a procedure provides a quantitative estimation of cellular populations in a given area of the tumor section.

The procedure devised by Chalkley, however, does not restrict itself to a few microscopic fields but permits a representative analysis of the whole specimen, in the present instance the non-necrotic portions of the tumor. Since not all the cells in the fields are counted, subjectivity is eliminated by counting only those cells which are indicated by the pointers. Further experiments are in progress which will permit a more accurate statistical evaluation of this work.

#### Summary

The growth rates of mammary adeno-

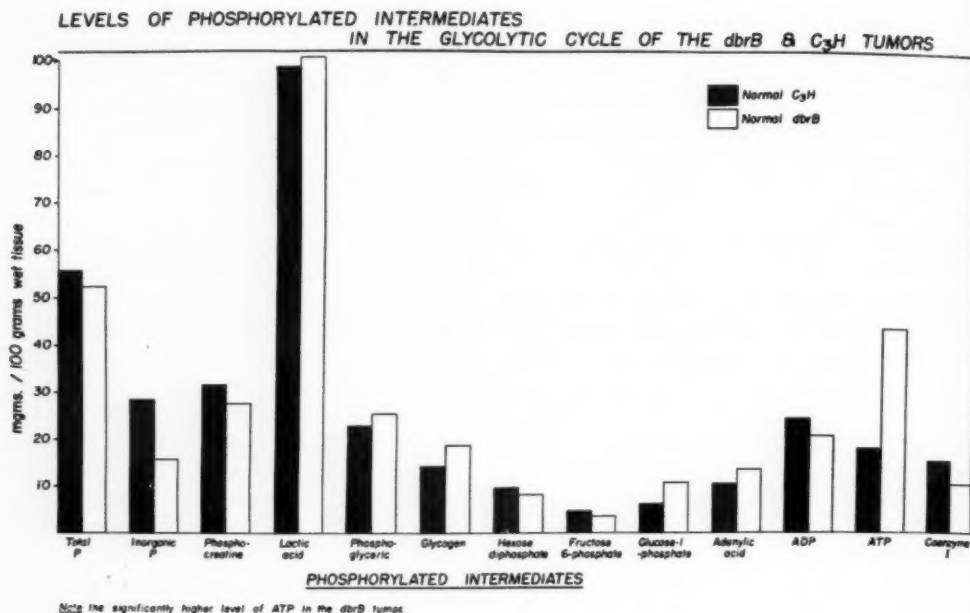


Figure 4

carcinomas of the dba and C<sub>3</sub>H strains of mice, referred to in the text as the dbrB and C<sub>3</sub>H tumors, respectively, were studied before and after irradiation. Chalkley's method, which permits a quantitative evaluation of spatial distribution of tissue components, was adapted for this study. The ratio of the number of actively dividing to resting cells (mitotic index) was taken as the criterion.

An average mitotic index of 1:49.6 (range, 1:43.8-1:53.8) was obtained for actively growing dbrB tumors, and an average mitotic index of 1:72.5 (range, 1:63.6-1:87.5) was obtained for the C<sub>3</sub>H tumors.

A depression in mitotic activity in the irradiated tumors was noted, the extent of which depended upon the dose of radiation applied and the lapse of time between exposure and removal of the tumors for analysis. An earlier and more pronounced return of mitotic activity was noted in the faster growing dbrB tumor following sublethal doses of radiation, as compared with the slower growing C<sub>3</sub>H tumor.

The results obtained indicate the possibility of applying Chalkley's method to a quantitative evaluation of growth activity

of tumors before and after irradiation, taking the mitotic index as the criterion. This method may also prove to be a helpful guide in clinical radiation therapy.

## II. THE INTERMEDIARY METABOLISM OF THE CONTROL AND IRRADIATED TUMORS

A previous study (19) has shown that the two analogous mammary adenocarcinomas, dbrB and C<sub>3</sub>H, described in Part I of this paper, differed significantly in their respiratory and aerobic glycolytic activity *in vitro*. In order to account for these differences it was deemed of interest to investigate their intermediary metabolism as it occurs *in vivo*. In this phase of the investigation the levels of the phosphorylated compounds in the Embden-Meyerhof glycolytic cycle were chosen as a criterion. Quantitative determinations of the various components in this cycle were made by the use of the freezing technic, and by enzymatic and chemical methods. Freezing the tumor tissue, either with liquid air or with dry ice-ether mixture, while still in the animal host or immediately after removal, permits a quantitative determination of the various metabolites as they oc-

TABLE V: PHOSPHORYLATED INTERMEDIATES IN C3H AND dbrB TUMORS\*

	C3H Tumor			dbrB Tumor		
	N	Mean	S.E.M.	N	Mean	S.E.M.
Total phosphorus	22	55.8	±3.29	27	52.2	±1.34
Inorganic phosphorus	22	28.2	±2.78	25	15.9	±1.12
Phosphocreatine	17	31.6	±4.50	17	27.6	±3.65
Lactic acid	20	98.8	±4.65	15	100.7	±4.51
Phosphoglyceric acid	21	22.9	±2.43	26	25.2	±1.49
Glycogen	15	14.1	±1.66	11	18.8	±2.27
Hexose diphosphate	22	9.3	±0.90	25	8.1	±1.00
Fructose-6-phosphate	22	4.9	±0.95	22	3.7	±0.31
Glucose-1-phosphate	20	6.2	±0.57	17	10.8	±1.68
Adenylic acid	19	10.6	±1.77	24	13.5	±1.16
Adenosine diphosphate	13	24.2	±4.80	18	21.7	±4.91
Adenosine triphosphate	12	18.0	±2.73	18	43.4	±4.30
Coenzyme I	14	15.3	±3.02	25	10.4	±1.10

\* Expressed in milligrams per 100 grams of wet tissue.

TABLE VI: PHOSPHORYLATED INTERMEDIATES IN dbrB TUMORS AFTER IRRADIATION\*

Dose, in Roentgens	Post- Irradiation Time	Total Phos- phorus	Inor- ganic Phos- phorus	Phospho- creatine	Lactic Acid	Phospho- glyceric Acid	Glycogen	Adenylic Acid	Adeno- sine Di- phos- phate	Adeno- sine Tri- phos- phate
10,000	21 hours	46.6	10.3	42.6	80.0	36.0	8.7	8.1	17.7	18.8
10,000	45 hours	48.5	11.8	22.0	106.5	18.2	20.3	10.6	11.2	42.4
10,000	7 days	41.6	13.6	30.6	118.6	19.3	(Not done)	20.4	8.8	50.6
10,000	10 days	40.6	12.3	37.7	90.9	18.4	(Not done)	11.0	5.2	38.2
12,000	22 hours	52.1	7.9	44.3	93.9	24.9	(Not done)	1.8	8.6	46.9
12,000 2 exp. (24-hr. inter- val)	5 days	49.4	9.4	29.5	74.8	40.2	33.6	12.1	8.9	51.3
20,000	21 hours	38.2	6.9	40.5	58.7	17.0	(Not done)	8.3	3.7	31.8
30,000 2 exp. (24-hr. inter- val)	68 hours	55.8	10.7	25.4	44.4	24.0	25.4	12.0	22.3	41.5

\* Expressed in milligrams per 100 grams of wet tissue.

cur *in vivo*. Details of the technical procedures used have been described at length in a report dealing with these tumors (20). Those pertinent to this paper will be described here.

Mice of the dba and C3H strains bearing young, actively growing tumors were immobilized by intraperitoneal injection of nembutal. To exclude the necrotic portions usually present in the center of the tumor, only surface portions of the actively growing tumors were dissected. These were immediately placed in either liquid air or in a dry ice-ether mixture. The frozen tumor tissue was pulverized by the use of a heavy piston in a specially con-

structed brass chamber and immediately used for analysis. Strict precautions were taken to keep the tumor material ice cold during analysis for all procedures requiring low temperature.

### Results

Levels of the components considered in phosphorylative glycolysis obtained from 27 analyses carried out on dbrB tumors and from 22 analyses carried out on C3H tumors are presented in Table V and Figure 4. A comparison of results reveals significant differences between the dbrB and C3H tumors in their mean values of inorganic phosphorus, glucose-1-phosphate,

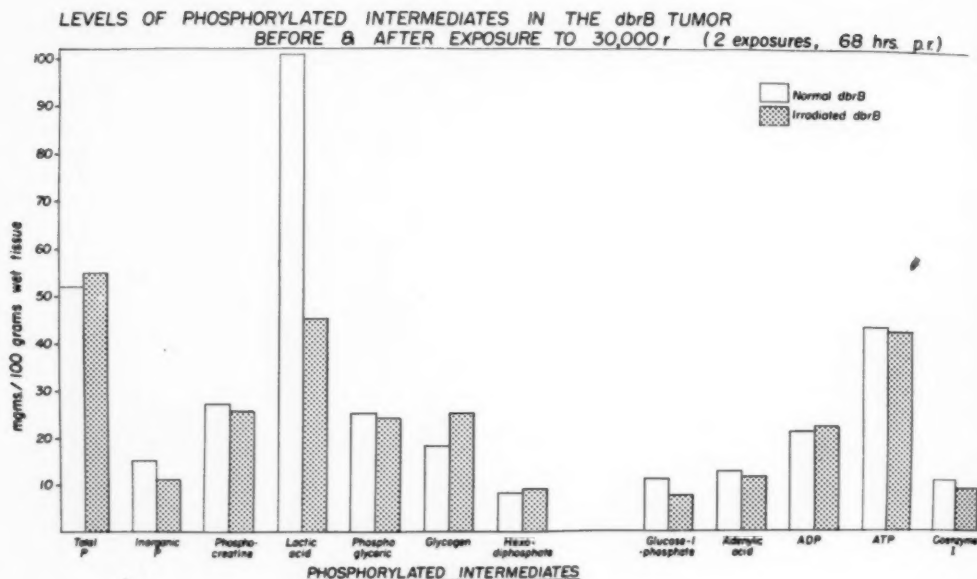


Figure 5

and adenosine triphosphate; the difference in glycogen is almost significant (c.r.,<sup>4</sup> 1.94). The higher glucose-1-phosphate level in the dbrB tumor (c.r., + 2.8) suggests a more rapid rate of glycogen breakdown in that tumor. It was also noted that the dbrB tumor has a lower level of inorganic phosphorus than the C3H tumor (c.r., - 3), and a higher level of adenosine triphosphate (c.r., + 5). These findings strongly suggest that a higher energy level is available for vital functions in the dbrB tumor. They lend further support to the previous observations that significant physiological differences exist between these two tumors although morphologically they are closely similar.

A series of experiments was carried out on irradiated dbrB and C3H tumors using the technical procedures that were employed with the controls. In brief, young, actively growing tumors (dbrB and C3H) were exposed *in vivo* to various doses of x-radiation, with the factors described in Part I (p. 847). Portions from the edges of three or four tumors were taken for each

analysis, as was done also in the control series. This phase of the work is still in progress but several pertinent results warrant discussion at this time.

dbrB tumors exposed to a single dose of 10,000 r were removed twenty-one hours, forty-five hours, seven days, and ten days following irradiation and analyzed for various components encountered in the phosphorylative glycolytic cycle. A comparison of the data thus obtained (Table VI) with those for control tumors (Table V) reveals a slight decrease in the adenine compounds (adenosine diphosphate and adenosine triphosphate) and in the lactic acid content twenty-one hours following irradiation. Results obtained forty-five hours, seven days, and ten days following exposure to the same dose fall within the normal range. These results indicate a temporary effect occurring within twenty-one hours following exposure to 10,000 r. Similar results were obtained from tumors analyzed twenty-two hours and five days after irradiation with 12,000 r applied in one or two exposures at twenty-four-hour intervals.

Tumors irradiated with 20,000 r in one

<sup>4</sup> Critical ratio.



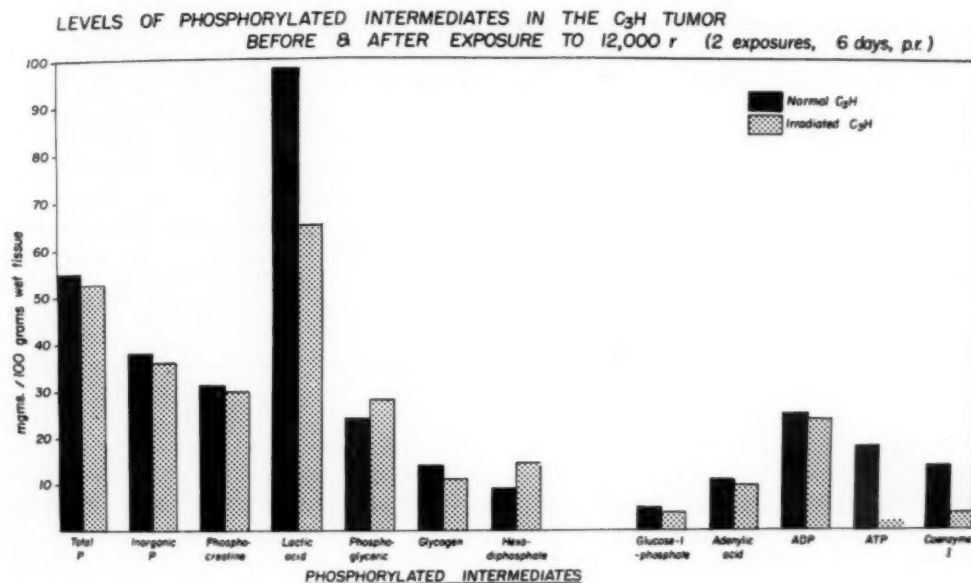


Figure 6

exposure and analyzed twenty-one hours later showed a decrease in lactic acid of about 50 per cent and a small decrease in adenosine triphosphate and in adenosine diphosphate.

Three experiments were carried out with a dose of 30,000 r applied in one or two exposures (15,000 r each at a twenty-four hour interval) with no marked change in the levels of the phosphorylated compounds. For example, the dose applied in two exposures to tumors which were analyzed sixty-eight hours later resulted in about a 50 per cent decrease in lactic acid but had no appreciable effect on the levels of the other compounds (Fig. 5).

A number of determinations of the phosphorylated intermediates of the irradiated C<sub>3</sub>H tumor were carried out simultaneously. It should be recalled that doses ranging from 8,000 to 12,000 r proved to be destructive for the growth of this tumor *in vivo* (21). It was of interest to determine whether doses within this range would affect the glycolytic cycle of the tumor. C<sub>3</sub>H tumors irradiated *in vivo* with a dose of 10,000 r and removed forty-six hours after irradiation showed no marked change

in the values of the compounds encountered in the phosphorylative glycolytic cycle, while tumors analyzed five days following irradiation showed a decrease in lactic acid content and a significant decrease of adenosine triphosphate; other compounds remained within the normal range. Similar observations were made with tumors analyzed six days after irradiation with 12,000 r applied in two exposures (Fig. 6).

#### Discussion

The results herein reported emphasize two points of interest. In the first place, these two analogous mammary tumors showed a significant difference in response of the adenine compounds to irradiation, those of the slower growing C<sub>3</sub>H tumor being more readily affected. In the second place, it is evident that to affect the metabolic processes, huge doses of radiation are required. As brought out in Part I, large doses are necessary to destroy the proliferative capacity of the tumors but, as shown above, still larger doses are necessary to affect their metabolic capacities. The necessity for large doses for total tumor destruction and a method for their possible

application will be discussed in Part III of this communication.

As reported (21), doses ranging from 16,000 to 24,000 r were destructive for the dbrB tumor, and doses of 8,000 to 12,000 r for the C3H tumor, depending upon the size of the tumor. That no marked effects were exerted by similar doses on the phosphorylative glycolytic cycle substantiates the observations, made by a number of investigators, that much larger doses are required to affect the metabolism of tissues, normal or malignant, than to affect proliferation. Huber (22), for example, showed that a dose of 12,000 r applied to the developing chick embryo caused a decrease in growth but had no effect on glycolysis. Löw-Beer and Reiss (23), using the Jensen rat sarcoma, found no quantitative change in anaerobic glycolysis, but the rate of aerobic glycolysis was slightly reduced following a dose of 650 R. Scott (24) concluded that a dose of 16,000 r applied *in vivo* and a dose of 100,000 r applied *in vitro* to frog heart muscle had no appreciable effect on respiration and carbohydrate breakdown to lactic acid.

Barcroft *et al.* (25) noted that the glycolysis of Walker rat carcinoma and Philadelphia-1 rat sarcoma were unaffected by doses of radiation that caused inhibition of their growth. Similar observations were made by the writer in experiments with mouse sarcoma 180 (26). On the other hand, a number of investigators using aqueous solutions of crystalline enzymes noted inactivation of the enzymes following exposure to very small doses of radiation. Thus, Forssberg (27) inactivated catalase in aqueous solution with 5 r. However, the addition of fumaric acid or cystine to the aqueous solution protected the enzyme to a great extent. Dale (28), in his experiments using carboxypeptidase, noted complete protection against inactivation of this enzyme by irradiation when nucleic acid or various sugars were added as substrate to the aqueous solution. Dale also showed a dependence of the effectiveness of radiation dosage upon the concentration of the enzyme in solution. For example, 50 r in-

activated about 30 per cent of a dilute solution, whereas a dose of 100,000 r was required to produce the same percentage effect on a solution 345 times as concentrated. Similar observations were made by Evans *et al.*, using sperm as an experimental object (29).

Efrati *et al.* (30) were able to destroy the activity of tetanus toxin with a dose of 7,000,000 r. Lower dosages, such as 4,000,000 r, partially reduced the activity of the toxin. The addition of 10 per cent albumin to the medium completely blocked the inactivating effect of 4,000,000 r on the toxin, while the addition of 0.1 per cent albumin was without demonstrable influence in this respect. No protective action was observed on the addition of globulin, casein, or irradiated toxin.

Barron *et al.* (31) noted that inactivation, by radiation, of sulfhydryl enzymes, *i.e.*, those requiring SH-groups in the protein moiety, can be reduced by adding glutathione to the medium.

The experimental data mentioned above, which were obtained on homogeneous, isolated biological objects, indicate the complexity of radiation effects when heterogeneous biological objects are used. They shed light on the question of why tremendous doses of radiation are necessary to affect metabolic processes of such complex systems as mammalian tissues, whether normal or malignant. The knowledge of the qualitative and quantitative relationships of components involved in such systems might help in the evaluation of their radiosensitivity.

#### Summary

The levels of the phosphorylated intermediates in the glycolytic cycle for two mouse mammary adenocarcinomas, dbrB and C3H, were determined. The more rapidly growing mammary tumor (dbrB) shows significantly higher levels of glucose-1-phosphate, adenosine triphosphate, and possibly glycogen, and a lower level of inorganic phosphorus than the slower growing C3H tumor. These findings strongly suggest that a higher level of energy is

available for vital function in the dbrB tumor.

Some of the compounds encountered in the phosphorylated glycolytic cycle, particularly adenosine triphosphate, may be more readily affected by irradiation in the C3H tumor than in the dbrB tumor. The metabolic processes were operative even after such large doses as 30,000 r for the dbrB tumor and 12,000 r for the C3H, although these doses proved to be lethal for their respective growth activities.

The large doses of radiation required to affect the metabolic processes and the mechanisms involved are discussed.

### III. THE FEASIBILITY OF APPLYING LARGE DOSES OF ROENTGEN RADIATION BY THE USE OF SMALL AREAS

Experimental data presented in Parts I and II point to the necessity of large doses of radiation for cellular destruction *in vivo*. As was shown by a number of investigators, including the writer, still larger doses are necessary for destruction of mammalian tissues, both normal and malignant, grown *in vitro* (32-38). Judging from these findings, it appears that progress in radiotherapy of malignant tumors calls for a technic which would allow the application of the necessary large doses without excessive injury to the host. Consequently, experiments were conducted on various shielding devices. By utilizing a lead shield enclosing the entire animal and applying the radiation through a small portal exposing only the tumor, the writer found it possible to apply the required high dose. The results were successful to a marked degree. In this way it was possible to apply the unprecedentedly high dose of 24,000 r, resulting in total destruction of a very radioresistant mouse mammary adenocarcinoma without injury to the rest of the animal organism. Moreover, the usual radiation sickness syndrome was virtually absent following treatment. In addition, the cured mice continued to produce normal litters, testifying to the reliability of the shielding device (39-40).

The explanation of these results lies in

the use of small portals whereby only small areas of the skin are exposed, diminishing the relative quantity of scattered x-rays and thus reducing skin damage. The writer took advantage of such occasions to advocate the use of large doses, when necessary, for human cancer, to be applied through a multiplicity of small portals. It was of particular interest, therefore, to learn, from an article published by Grynkrant (41), that attempts were made in this direction. His paper, in addition to a theoretical discussion on the mechanisms of radiation effects on biological material, includes a description of a technic for clinical radiotherapy consisting in the use of a grid made of lead, 2 mm. thick, in which 1.0-cm. square holes are cut 0.5 cm. apart, in a checkerboard pattern. The grid, lined with aluminum foil to filter off the soft secondary radiation from the lead, is placed directly on the area to be exposed. With protection of portions of the skin within this area, a larger dose can be applied without excessive damage to the skin and its vascular system. Grynkrant recommended that the same skin areas be protected throughout the course of treatment. In this way, the uninjured bordering vascular septa and stroma can enhance the recovery of those areas injured by irradiation, thus increasing the skin tolerance. Moreover, physical measurements involving the use of photographic film and a water phantom showed that the secondary rays emitted by the water during irradiation gave practically no image of the outline of the grid at a depth of 10 cm., thus providing evidence that, at a certain depth, a more or less uniform distribution of the rays takes place. This region in which there are no distinct zones of separation between the irradiated and non-irradiated areas, such as occur on the surface, represents the deep action of the roentgen rays. It follows, therefore, that the use of a grid permits less scattering on the surface and a diffuse distribution of radiation in the deeper layers. Such a situation is very advantageous for the treatment of deep-seated tumors; since

the skin is protected to a certain extent, larger doses can be applied, and consequently the deep-seated lesions receive larger doses relative to skin exposure.

Grynkrant used this technic on a number of cases and reported the details of a typical case in which the grid method had been used successfully on a patient having cancer of the liver (42, 43). A number of investigators (44-46) reported attempts to treat tumors by the use of similar grids previous to Grynkrant's work. Grynkrant, however, appears to have been the first to obtain successful results in man with this technic, probably because he used larger doses and an improved grid design.

Stimulated by Grynkrant's work with the small-portal technic on cancer patients, as well as by her own findings on the use of small portals in animal experimentation, the writer followed up the work on the validity of the small portal method in human cancer cases. The radiation therapist at the Cancer Hospital, New York City, was persuaded to apply this method to advanced human cases. To facilitate matters, the writer suggested that the grid be made of lead-rubber (47). With this modification, the procedure followed was essentially that of Grynkrant. Moreover, since favorable results had been obtained with a total dose of 24,000 r on a very radioresistant animal tumor (40),<sup>5</sup> it was suggested that such a dose be tried in the human cases. This total dose of 24,000 r, applied fractionally, was reported (48) to produce favorable results without excessive complications. More recently, treatments with similar large doses, using the grid technic, have been initiated in a number of other radiation therapy centers, and results, communicated personally to the writer, are also favorable.

It should be pointed out that the dose of 24,000 r currently being used clinically with the grid method was based on a measurement of the dose required in a small portal treatment to destroy a specific type of mouse mammary adenocarcinoma. In

recent publications (40, 49, 50) it was brought out that tumors, even of very similar morphological structure, may differ widely in their biological characteristics (rate of growth, metabolic activity, etc.). Since these characteristics play a great role in influencing the radiosensitivity of a tumor, it is to be expected that human neoplasms of similar morphological types may also differ in regard to the total dose requirements. This important feature should be taken into consideration in any method of treatment.

Another point of importance in the use of the grid method is the existence of an x-ray shadow from the grid for some distance into the tissue. In other words, although a lateral spreading of radiation occurs as one goes deeper into the tissue, because of tissue scattering, there exists the possibility that some portions of the lesion directly below the shielded portions of the skin will receive little or no radiation. Reference is made (40, 47) to observations which have demonstrated that growth may continue at the edge of a regressed tumor following irradiation, indicating that some tumor cells under the shielded area did not receive a lethal dose. The design of the grid, therefore, should be considered in relation to the depth of the lesion so that the penetrating dose is well distributed throughout the tumor.

Jolles (51, 52), in his investigations with superficially accessible tumors, such as those of the skin and breast, stresses the significance of the small-portal method for preserving the connective-tissue structures, thus enhancing recovery of the normal tissues within the exposed areas following irradiation. He recommends alternating the position of the grid after a series of treatments is completed; so that the previously unexposed areas are subsequently irradiated and all areas thus receive an equal dose. Such a procedure may also prove effective for treatment of deep-seated tumors.

In summary, the advantages of the small-portal method in radiation therapy are:

<sup>5</sup> This work was presented at the annual meeting of the Radiological Society of North America in 1948.



(a) It permits the application of large doses to tumors without excessive damage to the normal tissues.

(b) The dose can be calculated on a more precise basis because of relatively less back-scatter.

(c) The results can be more precisely reproduced because the dose is applied under more accurately controlled conditions.

(d) It permits a comparison of experimental with clinical results.

A great deal of work remains to be done on the small-portal technic. It is hoped that the method, dormant for so long a time, will be thoroughly studied by widespread clinical application. Moreover, through close co-operation between physicist, radiobiologist, and radiotherapist, its validity and advantages will be established. Only with such cooperative efforts can the ultimate potentialities of the multiple small-portal method in therapy of neoplastic growth be realized in the shortest possible time.

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### Part III

### SUMARIO

#### Nuevos Estudios sobre la Radiosensibilidad de los Tumores Análogos, dbrB y C<sub>3</sub>H, de la Mama del Ratón

Ya había advertido antes el A. que, en los experimentos *in vivo*, el tumor mamario murino C<sub>3</sub>H era más radiosensible que el tumor análogo dbrB, mientras que *in vitro*, sucedía lo contrario. Se explicó esto, tomando por base que la mayor actividad metabólica del tumor dbrB fomentaba una reposición más rápida consecutivamente a la irradiación *in vivo*. Tratando de lanzar más luz sobre las inherentes características biológicas y fisiológicas de esos dos tumores, lleváronse a cabo los estudios presentados ahora.

Los primeros experimentos versaron sobre la velocidad del desarrollo de los tumores *in vivo* antes y después de la irradiación, tomando en cuenta para ello la

proporción de células carioquinéticas por células en reposo. El índice carioquinético promedió 1:49.6 para los tumores dbrB en desarrollo activo y 1:72.5 para los C<sub>3</sub>H. En los irradiados, se observó una baja de la carioquinesis, cuya intensidad dependía de la dosis de rayos y del plazo transcurrido entre la irradiación y la extirpación del tumor. Notóse un retorno más temprano y pronunciado de la carioquinesis después de aplicar dosis subletales de radiación en los tumores dbrB de desarrollo más rápido que en los C<sub>3</sub>H.

La segunda fase de este estudio consideró el metabolismo intermedio de los dos tumores, tal como ocurren *in vivo*. El tumor de desarrollo más veloz—dbrB—re-

veló niveles significativamente más altos de glucosa-1-fosfato, trifosfato de adenosina, y posiblemente glucógeno, y un tenor más bajo de fósforo inorgánico que el  $C_3H$ , lo cual sugería elocuentemente que en el dbrB hay un tenor mayor de energía disponible para la función vital.

Algunos de los compuestos encontrados en el ciclo glucolítico fosforilado, y en particular el trifosfato de adenosina, pueden ser afectados más fácilmente por la irradiación en el tumor  $C_3H$  que en el dbrB. Necesitaron dosis mayores de radiación para afectar el metabolismo del tejido neoplásico que para cohibir la proliferación del mismo. Los procesos metabólicos mostraron actividad tras dosis de 30,000 r para el tumor dbrB y de 12,000 r para el  $C_3H$ , aunque las mismas resultaron letales en lo tocante a la respectiva capacidad para el desarrollo.

Habiendo indicado los precitados estudios la necesidad de dosis más altas para la citólisis, el A. ideó una técnica que permitía entregar una dosis de 24,000 r a un tumor murino a través de una puertecita, resguardando a la vez el resto del cuerpo del animal. El éxito que acompañó a este procedimiento, junto con las comunicaciones en la literatura de técnicas de puertecita o rejilla, sugiere las ventajas del método para la radioterapia clínica. Las mismas parecen ser las siguientes: (a) Permite aplicar dosis masivas al tumor sin lesionar excesivamente los tejidos normales. (b) Puede calcularse la dosis con mayor precisión por ser menor la retrodispersión. (c) Pueden reproducirse con mayor precisión los resultados por aplicarse la dosis bajo fiscalización más exacta. (d) Permite comparar los resultados experimentales y los clínicos.

#### DISCUSSION

(Papers by Rosh and Green and by Goldfeder)

**Austin M. Brues, M.D.** (Chicago, Ill.): These two papers illustrate a worthy recent trend in cancer research, I believe. Dr. Rosh illustrates the growing clinical research approach to the cancer problem; Dr. Goldfeder is an experimental worker who evidences interest in research which has a more or less direct bearing on the clinical practice of radiology.

Regarding Dr. Rosh's paper, I am reminded of a principle which was considered very well established ten years ago. There were a number of such principles; perhaps one of the most firmly grounded was that, although a tumor may have its origin as a result of physiological and external influences, once it is established it is no longer susceptible to these influences. This we see is no longer tenable.

In the case of carcinoma of the prostate the story appears to be simple, one particular type of endocrine approach being the effective one. In cases of breast carcinoma, the situation is obviously somewhat more complicated, because sometimes one steroid and sometimes another with obviously different physiological effects may be the effective agent in any particular case. One can only guess why this is. We see that in younger individuals the more profitable approach is castration, while in the older patient estrogens may be beneficial.

If one were to make a guess as to what the operating mechanism might be here, one might suppose that the mammary tumor becomes established in some sort of endocrine climate to which it is adapted, and an upset in this climate (sometimes in one way, sometimes in another way, depending upon the particular tumor) may be the effective means of reducing its size and growth rate.

It might be interesting to speculate whether the effect of androgens on bone metastases may be related rather to metabolism of the bone than to metabolism of the tumor itself. I mention this with some hesitancy, because this would again suggest a principle in cancer which, up to the present, has been contrary to certain of the established principles.

Dr. Goldfeder has shown that two tumors behave paradoxically in the face of irradiation, in that the more rapidly growing one is not as susceptible to radiation *in vivo* as the other. She has suggested that possibly the treatment of toxic products of radiation by these two tumors may account for the difference. At the present time the toxic products of radiation which are best understood and recognized are the break-down products of water, such as the peroxides, most of which are oxidants. Their life in irradiated tissue is very brief indeed, so that one could not explain

their removal rates on the basis of differences in the blood supply with any degree of assurance. There is, however, reason to believe that there are other toxic end-products of radiation that may also be involved, which do not have the same extremely short life, and this is one of the important problems in radiobiology currently.

One might suggest a possible alternative hypothesis, although data at the present time fail to indicate whether it can be ruled in or out. We have learned recently that the toxic effect of radiation on the whole animal can be relieved if the animal is anoxic or is treated with certain reducing substances at the time of irradiation, and we know, also, that a tumor which is made ischemic during irradiation is less radiosensitive than one which is not.

This effect no doubt relates in some way to the toxic oxidation products which I have mentioned, and one might suggest the possibility that the tumor with the faster growth rate, more vigorous mitotic rate, larger blood supply, and much higher metabolism, might actually, because of its higher metabolic needs, be in a situation of oxygen need. Again this must be purely speculative. In any case, I think we can say that the mechanism of tumor regression by irradiation is not understood and that the valuable work which Dr. Goldfeder is doing may bring us some time to an understanding of it.

Dr. Goldfeder also shows that the mitotic index of the rapidly growing tumor is not higher in the proportion that it should be on the basis of tumor growth rates. This might be accounted for in two ways: First, one has to remember that these tumors are all the time necrotizing in places, as well as growing in other places, and that some of the mitoses may represent the production of new cells, but these cells are susceptible to death soon after they are formed.

Another thing which I think is important to bring out is that the mitotic index as seen in the fixed section does not necessarily mean rapid growth rate any more than the presence of a large number of automobiles in the central part of Chicago indicates that there is a large flow of traffic. It may also represent a traffic jam, and the duration of mitosis (which we do not directly see) directly influences the mitotic index when it is used as an index of growth rate.

Mrs. Stroud and Mrs. Rietz in my laboratory have been investigating the question of the duration of mitosis and how it affects the mitotic index in various tissues, including tissue cultures. In some cases it can be shown that, although irradiation decreases the multiplication of cells, the delay in mitosis is such that upon looking at a section one apparently sees a stimulation of growth.

**Friedrich P. Ellinger, M.D.** (Washington, D.C.): It gives me great pleasure to discuss

again one of Dr. Goldfeder's presentations before this society. Dr. Goldfeder, through continuous effort, has considerably enlarged our knowledge in the field of radiosensitivity of malignant tumors.

First, she demonstrated that histologically identical tumors, developing in two genetically different strains of mice, may differ in their respective radiosensitivity as much as one to two. In this way she has brought to our attention the importance of the genetic make-up of the tumor host for the problem of radiosensitivity. This experience was then amplified by demonstration of different growth rates and radiosensitivities of these two tumors *in vitro*. The faster growing tumor was found to be the more radiosensitive one. Studies of the metabolism of the two tumors revealed a higher rate for the faster growing tumor as indicated by its glycolytic power.

Today's presentation correlates these data with some histologic facts. The faster growing tumor has been shown to have, also, the higher mitotic activity. Using the very convenient method of Chalkley for the determination of the mitotic index, which is demonstrated in her exhibit, Dr. Goldfeder found that the rates of mitosis were 1 to 50 and 73, respectively. Today's presentation also offered more detailed information on the intermediate metabolites involved in the previously demonstrated differences of metabolic activity. It has been shown that there are further biochemical differences between these two tumors, the faster growing having about two and a half times as large adenosine triphosphate content.

The past and the present work of Dr. Goldfeder gives ample support to her plea for shifting the emphasis in determining tumor radiosensitivity from merely histologic characteristics to physiological properties. She is not alone in this recommendation. As early as 1939 Cathie, in England, pointed out that in his experience the inorganic ash contents of tumor tissue appeared to be a more reliable index of tumor radiosensitivity than the histologic appearance.

As in so many instances in the history of medical science, increased knowledge in one field is bought for the price of at least temporary uncertainty in other fields so far considered relatively well settled. This seems apparently to be the case with respect to the different behavior of tumor radiosensitivity *in vitro* and *in vivo*. As Dr. Goldfeder indicated, the faster growing, metabolically more active tumor, which was more radiosensitive *in vitro*, required a larger single dose of x-rays for its arrest *in vivo* than did the slower growing tumor. This discrepancy seems to be more apparent than true and may resolve itself through further studies with fractionated doses of x-rays and following the reactions over a period of time.

It might well be mentioned at this point that



clinical experience has amply shown that radiosensitivity and radiocurability may not go hand in hand. The attempt to destroy a tumor with one single dose, as in these experiments, is comparable to a curative effort.

But in trying to evaluate radiosensitivity from a single exposure producing complete destruction, we should remember experience obtained on a comparable, very radiosensitive organ, namely the testis; here as little as 50 to 60 r may produce considerable injury temporarily, but ten times this dose is required for complete arrest of function in one exposure. We are hoping for further clarification of these problems through the results of further studies by Dr. Goldfeder. Undoubtedly these studies will put the problem of tumor radiosensitivity on more firm ground and provide more adequate clinical methods for its determination.

Biochemical methods such as employed by Dr. Goldfeder, and most appropriate for such an endeavor, are, at least for the time being, not practicable in the clinic. It might, however, be worth the effort to include in our routine clinical procedures for the study of biopsy specimens the determination of the mitotic index. This apparently parallels numerous other inherent biological characteristics of malignant tissue, as indicated by Dr. Goldfeder. The use of some of the special staining technics for cell nuclei, in addition to the routine hematoxylin-eosin stain, could be accomplished without difficulty and might greatly facilitate such endeavor.

I should like to compliment Dr. Goldfeder for having contributed so considerably to an important chapter of radiobiology, almost single-handed.

**Dr. Rosh (closing):** Until about twenty or twenty-five years ago we were all satisfied with the five-year survival period in reporting series of patients with carcinoma of the breast. Today we have more patients alive and well for fifteen years or longer. In carcinoma of the cervix seven years is a more crucial period than five or ten, based on the number of recurrences and metastases we have observed.

In carcinoma of the breast, metastases or recurrences may be observed five, ten, fifteen and, according to some reports, twenty years after diagnosis and treatment of the original lesion. Some feel that in such cases they are dealing with a new tumor, but others consider that the first tumor has merely been dormant and is reactivated at this time.

Recently Dr. Garland published in the *Journal of the American Medical Association* a comprehensive report of results with steroid therapy. With this form of treatment in combination with

deep x-ray therapy we can offer relief of pain, make patients more comfortable, and help them to be useful to their families and communities as long as possible. Some of our patients lived five to ten years.

**Dr. Goldfeder (closing):** In respect to Dr. Brues' comments on the mitotic activity and oxygen uptake of these tumors, I would like to emphasize that I searched for a criterion which might reveal why the faster growing tumor was found to be more radioresistant when grown *in vivo*. The mitotic index, which I selected as a criterion, represents the number of cells in active division relative to the number of resting cells, and does not indicate the time necessary for division of the cells. As shown, an earlier and more pronounced return of mitotic activity occurred in the faster growing tumor following sublethal doses of radiation. This observation is contrary to the Bergonie-Tribondeau law, which states that "the strongest effect of radiation is exerted on the least differentiated cells and on those of greatest reproductive ability." This law has been recently questioned by several investigators; for example, by Doctor Jacobson of the Argonne Laboratories and by Doctor Tullis of the Navy Medical Research Institute, who noted that the least differentiated cells in the bone marrow are the most radioresistant; and by Doctor Glücksmann of the Strangeways laboratories in England, who pointed out that the law is based on normal, undifferentiated tissue cells, and does not necessarily hold true for malignant tissue cells, which are unable to differentiate. The results that I obtained from the studies on the faster growing dbrB tumor seem to support the views expressed by the investigators just mentioned. That rapidly growing anaplastic tumors offer little success in clinical radiation therapy serves as further support of this view.

In regard to the oxygen uptake: The experimental data which I have presented show that the faster growing dbrB tumor possesses a greater metabolic rate than the slower growing C3H tumor. As has been shown by several investigators, and by myself, in order to affect the metabolism of any tissue, normal or malignant, much larger doses of radiation are necessary than to prevent their proliferation. This is the reason that I suggested, as a possible explanation, that the greater metabolic activity of the faster growing tumor enhances the recovery process by allowing the toxic substances produced by radiation to be carried away at a more rapid rate. However, much more work has to be done in order to throw light on the mechanisms involved in radiation effects before definite conclusions can be drawn.

## Secondary Carcinoma of the Phalanges<sup>1</sup>

FREDERICK W. BRASON, M.D., EDWARD G. ESCHNER, M.D., SAMUEL SANES, M.D., and  
GUSTAVE MILKEY, M.D.

**S**ECONDARY CARCINOMA of the phalanges is uncommon. It may occur from pressure and direct invasion, or through metastasis. Each of these types of involvement is illustrated in the following cases, both of which possess special interest for the roentgenologist.

**CASE I.** *Secondary Involvement of Distal Phalanx of the Right Thumb by Pressure and Direct Invasion from Carcinoma of the Nail Bed:* W. P., a 35-year-old white man, was admitted to the hospital on Dec. 29, 1948, with pain and swelling of the right thumb. Four months prior to admission, the patient had crushed his thumb, and a hematoma had resulted. The pain and swelling were of one month duration.

On admission, the distal part of the right thumb was swollen. A sinus at the tip discharged cheese-like material; similar material issued from a crusted area under the nail. The thumb was painful and tender. Epitrochlear and axillary nodes were not palpable. The clinical impression was "possible primary tumor; possible tuberculosis."

A roentgenogram of the right thumb showed a soft-tissue defect on the dorsal thenar aspect of the tip, with partial undermining and destruction of the nail. In this area there was some increase in the soft-tissue shadow, extending downward and backward to the phalanx. The bulbous portion of the phalanx was almost completely destroyed (Fig. 1); it presented a scaphoid defect with sharply demarcated border. Toward the basilar portion of the defect, the bone was irregular with decreased density streaking inward toward the joint. The roentgenologic impression was "osteolytic lesion, probably malignant."

Under local anesthesia (Jan. 4, 1949), the distal phalanx of the thumb was amputated by disarticulation. Following an uneventful postoperative course, the patient was discharged Jan. 17, 1949.

**Description of Surgical Specimen:** *Gross:* The nail was missing in the dorsal thenar surface of the disarticulated phalanx over an area 1.4 × 0.5 cm. In this area and beneath the preserved nail, soft yellow granular material was present (Fig. 2). On sagittal section through the thumb, yellow nodular masses were found under the nail in the soft tissue, extending into the bone and destroying the terminal end of the phalanx (Fig. 3). *Microscopically* the lesion proved to be an infiltrating, highly mature, squa-



Fig. 1. Case I. X-ray films of thumb showing destruction of distal phalanx, Dec. 27, 1948.

mous-cell carcinoma with keratinization (Fig. 4) and with reactive inflammation in the stroma. It had its origin in the nail bed, which showed extensive ulceration. The carcinoma compressed and invaded bone. At its junction with the still remaining bone, there were chronic inflammation and fibrosis. Here loose fragments of bone were noted. New bone formation was not seen. Beyond this zone of carcinoma and preserved bone, the marrow was fibrous. Bony trabeculae were thick.

**Comment:** In 1939, Levine and Lisa (1) collected 19 cases of carcinoma of the nail bed from the literature. In 1948, Ellis (2) reported 3 additional cases; Bayer (3) added 2 cases in 1949, and Russell (4) 1 in 1950. Among the cases in the series of Levine and Lisa only one showed true invasion of a phalanx. In 2 others, the bone was involved by pressure. The 4 cases reported by Ellis and Russell, and 1 of Bayer's cases revealed extensive malignant invasion of a distal phalanx. Advanced carcinoma originating in the skin, and malignant melanoma, may also destroy phalanges secondarily.

**CASE II.** *Metastatic Involvement of the Distal Phalanx of the Left Middle Finger from Primary Bronchogenic Carcinoma:* S. P., a 60-year-old colored

<sup>1</sup> From Edward J. Meyer Memorial Hospital and the School of Medicine, University of Buffalo, Buffalo, N. Y. Accepted for publication in April 1951.

man, was admitted to the hospital June 30, 1948, because of pain in the chest. Other complaints included anorexia, weakness, cough, night sweats, and weight loss. For one month the distal portion of the left middle finger had gradually grown larger and become increasingly painful. There was no history of trauma.

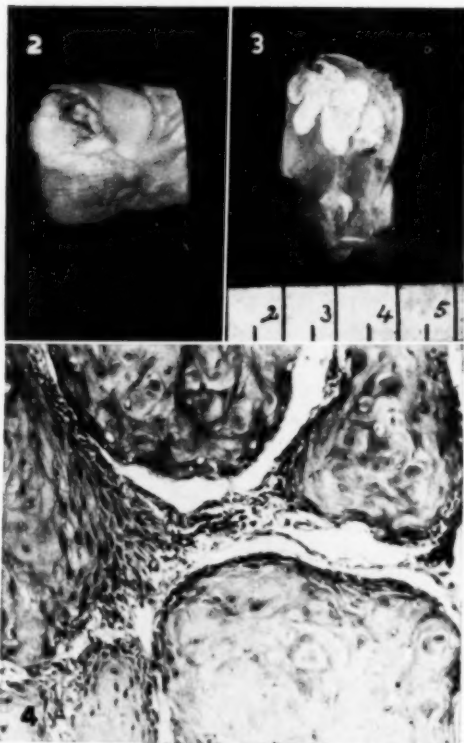
Examination of the chest showed dullness to flatness in the lower half of the left side, with decreased fremitus and breath sounds. The liver was palpable 4 cm. below the right costal margin. The distal third of the left middle finger was moderately swollen and tense; it was markedly tender.

X-ray films of the chest disclosed a density about the left hilus with a haze over the base of the left lung. The right hilus was broad and dense. Sputum and gastric washings were negative for tubercle bacilli. On bronchoscopic examination, the left main bronchus appeared fixed and narrowed; biopsy could not be obtained because of lack of cooperation of the patient. Needle biopsy of the liver was positive for metastatic, immature carcinoma.

An x-ray film of the left middle finger revealed a



Fig. 5. Case II. X-ray films of left middle finger showing destruction of distal phalanx, Aug. 5, 1948.



Figs. 2-4. Case I. External view of thumb showing tumor under nail (Fig. 2). Sagittal section of thumb with invading carcinoma (Fig. 3). Microscopic section showing mature squamous-cell carcinoma (Fig. 4).



Fig. 6. Cross sections through distal phalanx showing pseudocystic destruction of phalanx.

large area of increased soft-tissue density, limited mainly to the bulbous portion of the finger. It involved the entire pad of the finger and grew upward to produce a bulging of the nail. The distal phalanx was almost completely destroyed in its peripheral two-thirds. There was a round, rather excavated, defect on the thenar aspect of the bone with a thin, shallow rim of bone, irregular in contour, on the hypothenar aspect (Fig. 5). Considerable loss of bone density was apparent at the base of the distal phalanx down to the joint surface.

The clinical and roentgenologic impression was "bronchogenic carcinoma with metastases; chronic felon with osteomyelitis of left middle finger."

On Aug. 16, 1948, the left middle finger was amputated at the joint between the second and third phalanges.

*Description of Surgical Specimen:* Gross: The nail was intact. Cross sections (Fig. 6) showed destruction of the distal phalanx and replacement by a pseudo-cyst, filled with a serosanguineous fluid. The lining of the cyst appeared fairly smooth. Microscopically, the soft tissue and distal phalanx were seen to be involved by a metastatic, immature, infiltrating, medullary squamous-cell carcinoma (Fig. 7). The carcinoma showed central necrosis with pseudo-cyst formation. It grew in solid masses, surrounded by connective tissue. The stroma revealed reactive inflammation. Bone remained only in one small area at the periphery. Here, there was also osteoclastic bone destruction.

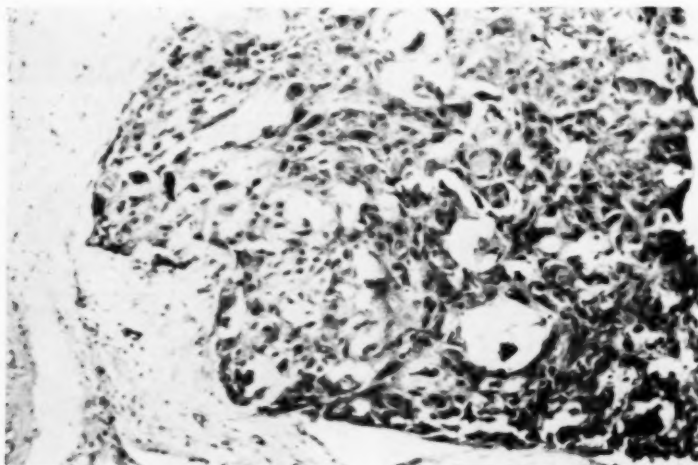


Fig. 7. Microscopic section showing immature squamous-cell carcinoma.

By Aug. 24, the amputation stump was well healed. The patient died Sept. 4, 1948. At autopsy, the diagnosis was bronchogenic carcinoma of the left lower lobe; metastatic carcinoma of liver, of mediastinal, hepatic, and retroperitoneal nodes, and of spleen; status following amputation of the distal portion of left middle finger (metastatic carcinoma); healed duodenal ulcers, nodular hyperplasia of prostate; small leiomyoma of stomach. No metastatic carcinoma was found in spine, ribs, or sternum. Postmortem x-ray films of the upper and lower extremities showed no metastases.

*Comment:* Like secondary carcinoma from pressure and direct invasion, metastatic carcinoma of the phalanges is uncommon. We have found 7 references in the literature (5-11), with mention of 13 cases. In most instances the metastases involved the phalanges of the hands. Primary sources included: parotid tumor, 1; carcinoma of the breast, 2; bronchogenic

carcinoma, 6; hypernephroma, 1; carcinoma of the uterus, 1; source not given, 2.

Clinical, roentgenologic, and pathologic details are available in only 6 cases, including our own, of phalangeal metastases from bronchogenic carcinoma (6, 8, 9). In this group, 5 patients were men. Ages ranged from forty-nine to sixty-eight years. Complaints referable to the metastatic lesion were more often rather sudden in onset than gradual. In 4 patients such complaints preceded the pulmonary symptoms.

In every case the metastatic lesion presented itself as an inflammatory process, with pain, swelling, redness, tenderness, and pulsation, so that the clinical impression comprised "whitlow," "paronychia," "infected bunion," "inflammation," "felon with osteomyelitis."

X-ray films consistently showed bony destruction, occasionally with soft-tissue changes. In one case new bone formation was noted. The adjacent joint was never affected. Involved bones were as follows: distal phalanx of the left fifth finger, of the left fourth finger, of the left middle finger, of the left thumb, and proximal phalanx of the right thumb and of the left large toe. In 3 cases bone other than the phalanges, in the feet and elsewhere, revealed metastatic lesions.



The pathologic diagnosis of the phalangeal lesion was made first by aspiration in 3 cases, by curettage in 1 case, upon amputation in 1 case, at autopsy in 1 case. The predominant histologic type of tumor was squamous-cell carcinoma. In 3 patients amputation was done for palliative effect; in one patient, x-ray treatment caused a decrease in size and tenderness of the lesion. Bronchogenic carcinoma as a primary source was proved by autopsy in 2 cases and through bronchoscopic biopsy and smear in 2 cases. In the remaining 2 cases the diagnosis was based on clinical and x-ray evidence.

#### SUMMARY

Two cases of secondary carcinoma of the phalanges in the hand are reported. Both were of special interest because of the roentgenologic findings. In the first case the phalangeal lesion was secondary to carcinoma of the nail bed; in the second, it was metastatic from bronchogenic carcinoma.

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#### SUMARIO

##### Carcinoma Secundario de las Falanges

Los 2 casos descritos son de carcinoma secundario de las falanges de la mano. En el primero, la lesión falangiana era secundaria a carcinoma de la matriz de la

uña; en el segundo, era metástasis de un carcinoma broncogénico. Las radiografías revelaron en ambos osteolisis y alteraciones de los tejidos blandos.

## Primary Melanosarcoma of the Esophagus<sup>1</sup>

JACK M. BURNETT, M.D.,<sup>2</sup> and ELMER ST. JOHN, M.D.<sup>3</sup>

MELANOSARCOMA of the esophagus is an extremely rare tumor. A review of the literature has revealed only four cases primary in the esophagus (1) and but one case of stenosing secondary melanosarcoma (2). The following case is presented as one of primary esophageal melanosarcoma.

### CASE REPORT

M. I., a 55-year-old white housewife, was admitted to the Johns Hopkins Hospital with a history of 45 pounds weight loss and regurgitation of food following meals for the preceding six months. She had been conscious of hoarseness and a slight cough for two weeks. She could take fluids much more easily than solid foods. Clinical signs of parkinsonism had been present for twenty years.

Physical examination was negative except for the parkinsonism. There was no evidence of tumors of the skin or eyes. The serologic test for syphilis was negative. The hemoglobin was 13.5 gm. per cent. The stools were guaiac-positive. The urine contained no sugar, albumin, or formed elements.

Repeated esophagrams demonstrated at the junction of the middle and lower thirds of the esophagus a mass measuring approximately 7 × 5 cm. The surface of the mass appeared smooth and there was no evidence of invasion of the contiguous esophageal wall. Above the mass the esophagus was dilated, and beyond it there was only a slow, small trickle of barium (Fig. 1).

Numerous other diagnostic procedures, including several unsatisfactory esophagoscopy examinations, failed to clarify the nature of the apparent neoplasm.

Nine days after admission an exploratory thoracotomy was performed. The lower end of the esophagus, including the tumor (Fig. 2), was resected and the proximal end of the esophagus was anastomosed to a new site in the cardiac end of the stomach. The postoperative course was smooth for the first two weeks, at the end of which time signs of phlebitis, pulmonary thrombi, and pulmonary infarction developed. The patient gradually recovered and was discharged from the hospital about seven weeks after operation.

A follow-up examination approximately eight months postoperatively was reported as "a negative barium swallow." No obvious tumor metastases



Fig. 1. Spot film of esophagus showing obstructing mass.

were noted, although there had been a considerable loss of weight. The patient died at home two months later, following an episode that was clinically thought to be a subarachnoid hemorrhage. No autopsy was obtained.

*Gross Description of Tumor* (Dr. Stanton Eversole): The specimen consists of a portion of the esophagus which measures 7 cm. in length. Attached to the mucosal surface is a pedunculated tumor 7 cm. in length and 5 cm. in width, protruding 3.4 cm. into the esophagus. The tumor itself is very soft and coal black. Its smooth surface contains some lobulations. At its base one can see no evidence of deep invasion of the esophageal wall. There is apparent scarring of the esophageal wall underlying the tumor. Several periesophageal lymph nodes contain the same black tumor material.

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**Microscopic Description:** The tumor is composed of large, pleomorphic cells. The cytoplasm is abundant and takes a slight basophilic stain. Large numbers of cells are filled with brown to black pigment. The nuclei are quite large and pleomorphic, containing clumps of chromatin and conspicuous nucleoli (Fig. 4). At the tumor edge, the neoplastic cells extend for some distance under the esophageal epithelium and form infiltrating masses containing little pigment. The surface of the mass is ulcerated and in one section tumor is found deep in the esophageal muscularis (Fig. 3). The lymph nodes contain tumor.

**Diagnosis:** Melanosarcoma of the middle third of the esophagus, with metastases to adjacent lymph nodes.

#### COMMENT

In the absence of evidence of a primary melanosarcoma elsewhere in this patient, we are probably justified in considering this tumor primary in the esophagus. As we have already pointed out, even metastatic melanosarcoma of the esophagus is rare. Among the first 22,000 autopsies performed at the Johns Hopkins Hospital, there were 25 cases of melanosarcoma. In not one of them was tumor seen in the esophagus, either primary or metastatic. This absence of esophageal metastases is especially remarkable because in some cases almost no other organ was spared.

Jaleski and Waldo (1) added their case to the three previously reported cases of primary esophageal melanosarcoma. They pointed out that none of the cases, including their own, was correctly diagnosed during life because the esophageal lesion did not cause obstruction. Our case was diagnosed because it did cause obstruction. Interestingly enough, the only case reported of probable metastatic esophageal melanosarcoma also produced obstruction (2).

#### SUMMARY

A case of rare primary melanosarcoma of the esophagus causing obstruction is described.

NOTE: The photographs for this paper were made by Miss Joan Wheaton.

Veterans Administration Hospital  
Fort Howard, Md.

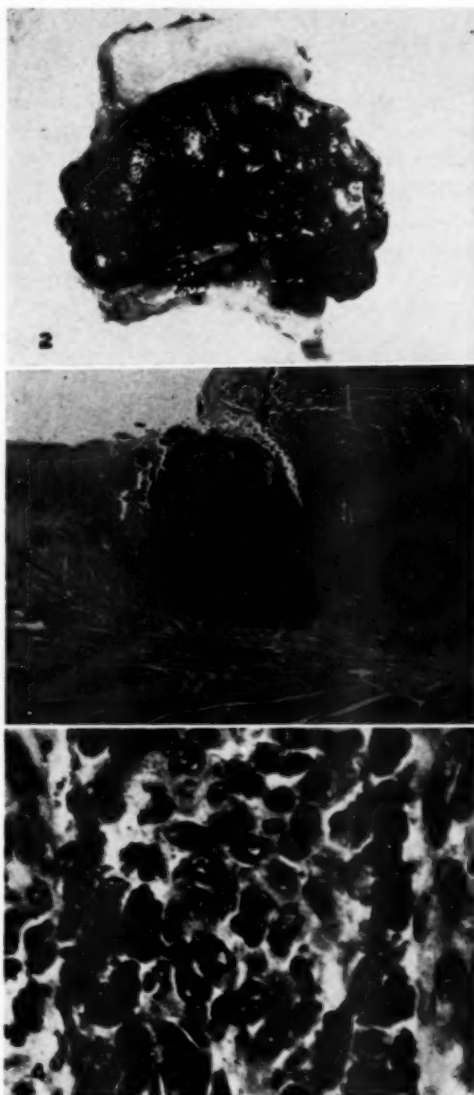


Fig. 2. Removed esophageal segment and tumor.

Fig. 3. Low-power view of tumor edge and esophageal mucosa. Note tumor ulceration and submucosal infiltration.

Fig. 4. High-power view of tumor. Note large, pigmented and non-pigmented tumor cells.

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## SUMARIO

**Melanosarcoma Primario del Esófago**

Descríbese un caso de melanosarcoma que parecía ser primario en el esófago, elevando así a cuatro el total de melanosarcomas primarios del esófago que aparecen en la literatura. El diagnóstico de tumor oclusivo se hizo roentgenográficamente, confirmándose histológicamente la naturaleza del mismo.





# Roentgenologic Considerations in Tracheo-Esophageal Fistula Without Esophageal Atresia

With Report of Two Cases<sup>1</sup>

TED F. LEIGH, M.D., OSLER A. ABBOTT, M.D., and WILLIAM A. HOPKINS, M.D.

THE PURPOSE of this communication is to present two cases of congenital tracheo-esophageal fistula without esophageal atresia which have not been previously reported, and to discuss some roentgenologic considerations of this rare and interesting anomaly. The fistulous tract in each case was visualized roentgenoscopically and recorded on roentgenograms. In each instance the tract was repaired.

In most reported cases, the fistulous tract has arisen from the anterior wall of the esophagus and extended to the posterior wall of the trachea; in one case, the communication was with the left main-stem bronchus. The esophageal and tracheal openings of the fistulous tracts have varied from the size of a pinhead to several millimeters in diameter.

The incidence of this lesion among all types of tracheo-esophageal anomalies is reported as 3 to 10 per cent, but judging from the few articles dealing with fistula without atresia, would seem much less. The diagnosis is made more often at postmortem examination than during life. This state of affairs can be reversed only by a high index of suspicion in the minds of the referring physician and the radiologist.

## REVIEW OF THE LITERATURE

The literature on the subject of tracheo-esophageal fistula without atresia is scant.

Haight (1) has written the most comprehensive survey to date. He cites articles by Lamb, who published a case in 1873, by Cautley, who found six instances of the lesion up to 1917, and by Plass, who in 1918 discovered only 1 example in 136 reported cases of malformations of the esoph-

agus. Haight himself found 2 cases of fistula without atresia and 63 with atresia in a twelve-year period at the University of Michigan Hospital. He reported one case, referred to him by Dr. Duane Carr of Memphis, Tenn., who had established the diagnosis. The patient was four years of age and had presented symptoms of choking and cyanosis concurrent with feedings since birth. On the second day after birth, a catheter was passed into the stomach; on the fourth day, barium was injected into the stomach through a catheter; on the twelfth day of life, barium was noted in the trachea and right bronchi following oral ingestion, but this was interpreted as a spill-over through the larynx. Atelectasis of the right upper lobe was noted at this time, and ensuing films over the next four years revealed varying degrees of bilateral pneumonitis. Cough and choking continued during this interval. In the fourth year, lipiodol was given with the child in the prone position (the mother had stated that the symptoms were more pronounced when the child was prone), and filling of the trachea and both main-stem bronchi was observed. On this basis, the diagnosis was made. Further radiographic studies carried out by Dr. Holt at Michigan showed similar findings, though the exact site of the fistulous tract could not be identified. The tract was surgically repaired and, at last reports, the boy was doing well.

Clerf (2) reported a case in a woman of 23, who gave a history of cough associated with swallowing of food and fluids for seven years. The diagnosis was made by esophagoscopy; after the tract was visualized, a catheter was passed into it, and a little

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iodized oil injected. Roentgenograms accompanying the article show the catheter and oil in the tract, and oil in some bronchial ramifications.

McKinney (3) had a patient 58 years of age who gave a long history of "sick stomach and vomiting spells," and recent paroxysms of coughing. Chest roentgenograms were negative, but following a gastro-intestinal series, barium was noted in the right bronchial tree. At bronchoscopy a minute opening was demonstrated at the lower end of the trachea, but on esophagoscopy the opening could not be found. No roentgenograms were made. McKinney compares his case to one of Negus, whose patient died of carcinoma (site undetermined) at 45 years of age, and who at postmortem examination was found to have a congenital fistula leading downward from the trachea to the esophagus; on the esophageal aspect was a small valve-like hood of mucous membrane, which must have prevented regurgitation.

Imperatori (4) reported the case of an 8-year-old child with a slit-like fistulous opening measuring about 1.3 cm. in length. This fistula was opposite the third, fourth, and fifth tracheal rings. A lateral roentgenogram of the cervical region shows a ureteral catheter passing from the trachea through the fistula into the esophagus. This tract was successfully closed.

Gengenbach and Dobos (5), in 1941, published a report of 10 cases of congenital tracheo-esophageal anomalies, in 3 of which there was "little, if any, esophageal obstruction." In one of these, the radiologist noted that "the barium passed freely into the stomach; some swallows, or portions thereof, entered the trachea above the fourth dorsal vertebra, and it passed into both main-stem bronchi." This tract measured 4 mm. in diameter. In the second case, roentgen studies were not conclusive, and at bronchoscopy a small orifice was noted 2 or 3 cm. above the bifurcation of the trachea. In the third case, a film was made after lipiodol injection into the esophagus and some contrast material "was seen in the left main-stem bronchus



Fig. 1. Case 1. The opacified lumen of the fistula is seen, extending from the anterior esophageal wall slightly upward to the posterior tracheal wall in its middle third. (Insert depicts tract's appearance.) The film was made with the patient in a right anterior oblique position in relation to the table. This position allowed visualization of the tract and the pattern of the tracheal opacification. The tract is slightly less dependent in this projection than if the patient were prone.

and trachea. No definite evidence of a fistula."

Leven and Lannin (6) had two cases of fistula without atresia in a series of 41 tracheo-esophageal anomalies. These are not reported in detail.

In 1946, Holt, Haight, and Hodges (7), discussing Vogt's classification of esophageal anomalies, stated: "To this group might be added that form of single tracheo-esophageal fistula which exists without esophageal atresia. This type is unusual and presents particular diagnostic difficulties." One case in their series of 45 tracheo-esophageal anomalies was a fistula without atresia. No elaboration is made on this case, except to say that gastric distention was greater than in any of the other 44 patients.

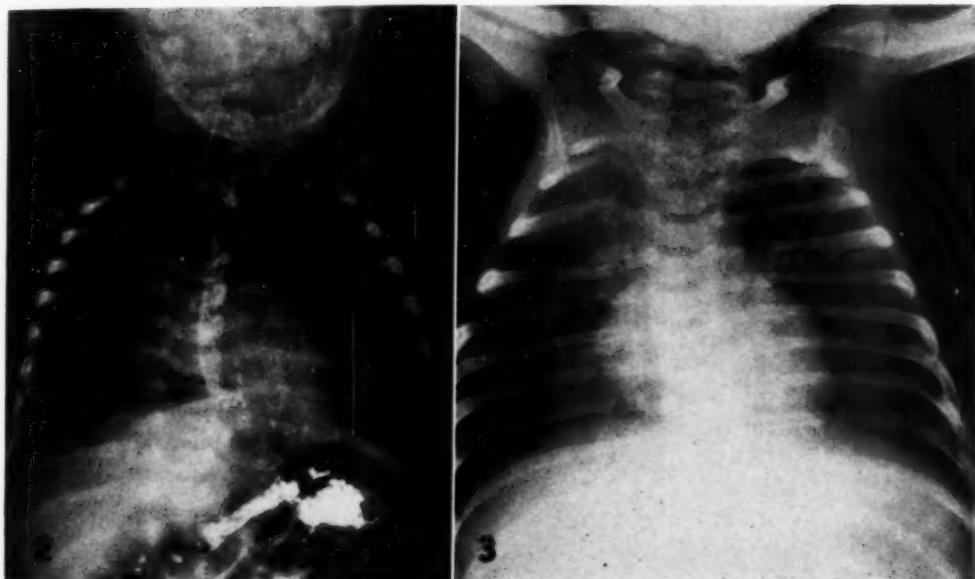


Fig. 2. Case 1. There are areas of consolidation in all three lobes of the right lung, probably caused by the aspiration of ingested material. The left lung is relatively free of disease. Very little of the opaque medium entered the right lung. Some is still present in the esophagus. Abdominal distention is greater than normal.

Fig. 3. Case 1. Chest roentgenogram two weeks after operation. The right-sided pneumonitis has persisted. Minimal disease is present in the left upper lobe. No opaque material remains. Abdominal distention is decreased.

Brown and Brown (8), in a review of 24 cases of esophageal anomalies between 1940 and 1949, stated that there had been "2 cases of congenital tracheo-esophageal fistula without atresia in the Buffalo Children's Hospital, not included in this series, one in 1931, the other in 1950." No details were given on these two cases.

The most recent article is that of Cardullo and Berens (9). With their patient in supine position, 2 c.c. of diodrast were injected through a high esophageal catheter with immediate opacification of the right and left major bronchi and their ramifications without regurgitation or aspiration of the contrast material. They at once suspected a fistula without atresia but, at the request of the surgical consultants, repeated the examination twelve hours later with lipiodol. On this occasion, no oil entered the bronchial tree. Later, post-mortem examination of the esophagus revealed a 3-mm. slit on the mid-anterior wall, and a tract extending into the trachea.

#### CASE REPORTS

**CASE 1.** M. J. B., a boy of 6 weeks, was admitted July 29, 1949. He had been apparently normal at birth, except that he choked on his feedings. At that time, a Levine tube was passed into the stomach by the pediatrician and no abnormalities were noted. Later, because of continued distress, radiographic studies were made and a diagnosis of tracheo-esophageal fistula without atresia was made.

Physical examination on admission was essentially negative except for some basilar pneumonitis.

**Roentgen Studies:** Roentgenoscopic examination with lipiodol revealed a small fistulous tract between the anterior wall of the esophagus and posterior wall of the trachea in its middle third (Fig. 1). The esophagus appeared otherwise normal. Most of the oil in the trachea was coughed up immediately, but small amounts entered the right lung. Here there were patchy consolidations, interpreted as aspiration pneumonitis (Fig. 2).

**Hospital Course:** On Aug. 1, bronchoscopy revealed a 3-mm. slit on the posterior tracheal wall, 1 cm. or less above the carina.

**Surgery:** On Aug. 3, a posterior incision was made; the fistulous tract was identified and transected.

**Postoperative Course:** Recovery from the fistulous tract repair was uneventful. The pulmonary infection, however, (Fig. 3), and an infection of the right side of the back and right thigh delayed recovery.

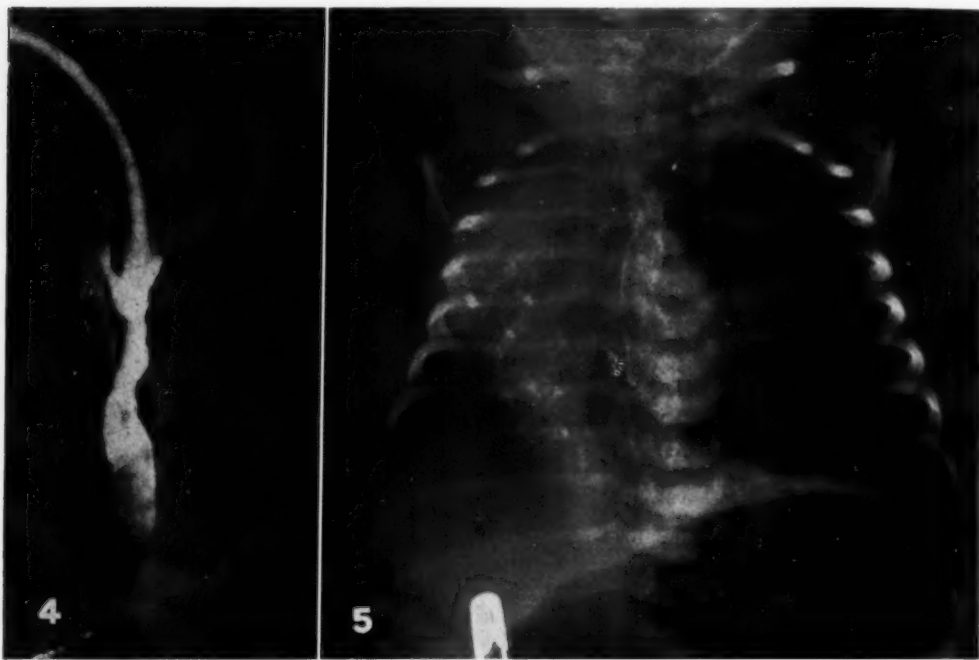


Fig. 4. Case 2. The fistulous tract, esophagus, and trachea are opacified. The tract resembles that of Case 1. The film was made in a similar manner to that in Fig. 1.

Fig. 5. Case 2. Moderate amounts of oil are seen in the right lung following aspiration through the fistulous tract. There is severe pneumonitis in the right lung. The left lung is relatively normal. Gastric distention is marked.

Skin grafting was necessary. At final discharge in November, the patient was healthy and gaining weight.

**CASE 2.** Baby B, a boy, born May 17, 1950, was delivered normally, cried immediately, and was admitted to the nursery in good condition. A short time later, cyanosis of the extremities was noted and oxygen was given. With the first feeding, the cyanosis became generalized. After aspiration of a considerable amount of mucus, a tube was passed into the stomach without difficulty by the pediatrician. Between feedings the color improved, but on feeding the cyanosis returned. Thick, copious material persisted and, because of rhonchi heard throughout both lungs, chemotherapy was instituted. On May 21, roentgenograms revealed patchy consolidations in the right lung. The patient was now jaundiced and pedal cyanosis was persistent. The pediatrician's progress note for this date read in part: "Catheter passage into stomach should rule out T-E fistula unless of an extremely rare type." Aspiration of amniotic fluid or a vascular ring seemed more probable, and, on the basis of the latter, a surgical consultation and a lipiodol swallow were ordered.

**Roentgen Studies:** Fluoroscopy was first done with the patient in supine position. A catheter was

passed into the upper esophagus, and on filling with lipiodol no abnormalities were noted. The child was then turned into the right anterior oblique position on the table and, when the iodized oil was instilled into the upper esophagus, there was simultaneous opacification of both trachea and esophagus. In the trachea, the medium was seen to fan out cephalad and caudad from a single focus. Closer observation showed an opacified fistulous tract extending from the anterior wall of the esophagus slightly upward to the posterior wall of the mid-trachea. Spot films were made immediately (Fig. 4). The baby was quickly turned head down but, despite this maneuver, some of the oil passed into the right lung. On a teleroentgenogram made after fluoroscopy, the aspirated oil appeared small in amount compared to that previously present in the trachea (Fig. 5).

**Surgery:** With the diagnosis made, the infant was prepared for surgery. A right lateral approach was used. A Penrose drain was slipped around the esophagus. The trachea was identified and, with dissection of the esophagus cephalad, a fistula was identified; it measured about 0.7 cm. in length and 0.5 cm. in diameter. It followed a downward course from the trachea and entered the esophagus at a lower level. This tract was divided and the ends



closed with 0000 silk. After chest closure, the patient was given 50 c.c. of blood and returned to his room in good condition.

**Postoperative Course:** On the second postoperative day, a tension pneumothorax developed when the thoracotomy tube became blocked. This was unplugged and the tension subsided. Eight hours later cyanosis and apnea suddenly developed without premonitory difficulty. Supportive measures were unavailing, and death ensued.

**Postmortem Examination:** The principal findings were extensive primary atelectasis in both lungs, moderately extensive bronchopneumonia in the right lung, and slight bronchopneumonia in the left. Careful examination of the surgical site revealed no breakdown of the repair, and only a minimal mediastinitis.

#### ROENTGENOLOGIC CONSIDERATIONS

For a successful roentgenologic demonstration of a tracheo-esophageal fistula without atresia, we feel that the following suggestions are helpful.

1. *Optimum positioning of the patient.* Because the fistulous tract originates on the esophageal wall anteriorly and extends to the tracheal wall posteriorly, some authors have stressed the use of a prone position for fluoroscopic examination; while it is true that in this position the tract is most dependent, there is the serious disadvantage that the opacified esophagus will completely hide the fistulous tract and probably obscure the pattern of the tracheal filling. We believe that anterior oblique positions (in relation to the table), either right or left, are far more satisfactory for the fluoroscopist and for his spot films, and that their advantages outweigh the disadvantage of having the tract slightly less dependent. In both of our cases, the published roentgenograms were made in the right anterior oblique position, in relation to the table top (left posterior oblique to the screen).

2. *Correct positioning of the esophageal tube.* The tip of the esophageal tube should be cephalad to the level of the carina and probably opposite the middle third of the trachea. The level of the fistula has varied considerably in the reported cases, and accurate positioning is difficult. An optimum rather than exact position must be selected.

Contrast material instilled into the lower esophagus most likely would miss the tract unless regurgitation occurred, and at such a time one is more likely to be preoccupied with preventing aspiration rather than producing it. Instillation of the medium directly into the stomach is of no consequence, as was shown in Haight's case.

3. *Proper selection of contrast material.* Barium, of course, should never be used when a tracheo-esophageal fistula is suspected. Iodized oil successfully demonstrated the tract in our two cases, but it may be unsuccessful in less patent tracts. Diodrast has been successful where lipiodol failed, as in the case reported by Cardullo and Berens. These authors observed that "a 35 per cent solution of diodrast is not irritating to the bronchial mucosa and affords the additional advantage of being rapidly absorbed (within twenty-four hours), leaving no lasting residuum in the respiratory tree, as the oil preparations do." Air instillation, used by Fuhrman *et al.*, (10) in demonstrating an esophageal pouch when atresia is present, would be impractical here, partly because of the small size of the tract and partly because of the obscuring air in the trachea, lungs, and esophagus.

Whatever the contrast material, we believe that its proper use is more important than its type. Theoretically, the tract is normally collapsed and must be opened by a sufficient quantity of the medium and by the force of its injection. A relatively large tract presents no difficulties unless it is protected on its esophageal side. A small tract with a pin-point opening may resist all attempts at dilatation.

One should, of course, allow no more medium in the trachea than is necessary to make the diagnosis. Fortunately, most of it is coughed out immediately rather than aspirated. Emptying of the trachea can be facilitated by inverting the patient.

4. *Proper interpretation of findings.* Characteristically, the tracheal opacification begins at the fistulous opening and spreads out cephalad and caudad. This



happens quickly and to us is a pathognomonic sign. It must not be interpreted as a spill-over through the larynx. Since the fistulous tract at this moment may be completely hidden by superimposition on the opacified esophagus or trachea, the radiologist may have to rely entirely on the sequence of events he has witnessed. If a diagnosis is not made with certainty at the first attempt and further investigation is indicated, sufficient time should be allowed for the trachea and esophagus to clear, or the "spreading" effect in the trachea may be obscured.

Pulmonary consolidation invariably accompanies fistula without atresia, being produced by aspiration of ingested materials through the tract. Probably the most important factor in pulmonary infection is the patency of the tract; less important, its diameter and duration. It is noteworthy that several of the reported cases were in the older age group and in these there was no pulmonary infection. In our two cases, pulmonary infection was more advanced in the week-old baby (Case 2) than in the one six weeks of age.

Interestingly enough, in both of our cases the right lung was predominantly involved by the inflammatory process. We believe that the slight difference in the angulation of the main bronchi is not as important in this as is the position in which the infants are kept when feeding and sleeping.

We further believe that the diagnosis of tracheo-esophageal fistula without atresia should be given serious consideration in any newborn infant with unexplained pneumonitis.

When a fistulous communication is suspected and is not proved by routine roentgenologic examination of the esophagus, the diagnosis may be established by a tracheogram. This is obtained by placing the patient supine on a radiographic table and rapidly instilling 1 or 2 c.c. of warm iodized oil into the upper trachea under laryngoscopic guidance. Four films are made immediately in antero-posterior, left lateral, right lateral, and postero-anterior projections. With good

technic, the entire trachea will be opacified. The opaque material should fill some or all of a fistulous tract if present, partly because the tract is dependent when the patient is supine (during the injection) and partly because the rigid tracheal wall will not collapse around the opening as the flaccid esophagus might. As mentioned above, McKinney in his case easily demonstrated a minute opening by bronchoscopy but was unable to find it on esophagoscopy.

Bronchoscopy and esophagoscopy are the most important non-radiological procedures in the diagnosis of tracheo-esophageal fistula without esophageal atresia; they alone will make the diagnosis when the openings are of sufficient size (2, 4). For smaller tracts, where identification is more difficult, Abbott (11) has suggested that methylene blue or a similar dye be instilled into the esophagus by catheter during bronchoscopy and its point of entry into the trachea sought.

#### SUMMARY

1. The available literature on tracheo-esophageal fistula without esophageal atresia is reviewed, particularly from the point of view of clinical symptomatology and radiological diagnosis. Few of the reported cases have been accurately diagnosed radiologically.

2. Two cases of tracheo-esophageal fistula without atresia are reported in detail.

3. Suggestions for improving the radiographic diagnosis of this type of anomaly are made.

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#### SUMARIO

#### Consideraciones Roentgenológicas en la Fístula Tráqueo-Esofágica sin Atresia Esofágica, con Presentación de Dos Casos

Repásase, en particular desde el punto de vista de la semiología y el diagnóstico, la literatura disponible sobre la fístula tráqueo-esofágica sin atresia esofágica. Pocos de los casos comunicados han sido diagnosticados con exactitud radiológicamente.

Descríbense aquí 2 casos, en ambos de los cuales el trayecto fistuloso entre el esófago y la tráquea era observable roentgenológicamente.

Sugiere que, para el éxito en la observación roentgenológica de la fístula tráqueo-esofágica, se preste atención a: (1) la posición óptima del enfermo (los AA. prefieren la oblicua anterior en relación con la mesa); (2) la posición correcta de la sonda esofágica, con la cánula dirigida ha-

cia la cabeza a la altura de la quilla del esternón y probablemente enfrente del tercio medio de la tráquea; (3) adecuada selección y administración del medio de contraste (en los casos de los AA. se usó aceite yodado); (4) debida interpretación de los hallazgos.

La hepatización pulmonar, debida a la aspiración de sustancias ingeridas a través del trayecto, acompaña invariablemente a la fístula sin atresia. Parece que este diagnóstico debe recibir consideración detenida en todo recién nacido con neumonitis inexplicada. Si se sospecha la existencia de una abertura fistulosa y no puede comprobarse con el corriente examen roentgenológico del esófago, puede establecerse el diagnóstico con un traqueograma.



## Pantopaque Meningitis Due to Hypersensitivity<sup>1</sup>

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THE DISCOVERY and wide utilization of pantopaque as a contrast medium in the study of lesions in and about the spinal canal has led to the realization that the substance is relatively safe but not entirely innocuous. Pantopaque (ethyl iodophenylundecylate) is a mixture of isomeric ethyl esters. The literature gives ample evidence that there is an inflammatory and proliferative meningeal reaction in certain instances following the introduction of the material intrathecally (1, 2). Systemic reactions with mild fever, headache, malaise, and cerebrospinal fluid changes, including increase in cell count and protein have been observed. These reactions have been immediate in onset and occasionally have been associated with demonstrable histologic changes in the leptomeninges (3). The reactions, however, have proved in almost all instances to be transient and have not been considered contraindications to continued use of the medium as a diagnostic aid. The purpose of this paper is to present evidence of meningeal reaction to pantopaque, delayed in onset and associated with certain phenomena which strongly suggest hypersensitivity.

Because of the occurrence of several severe reactions to the intrathecal injection of pantopaque, a procedure was instituted as a precaution against possible sensitivity. This consisted of the intradermal injection of 0.1 ml. of pantopaque and twenty minutes subsequent observation for the appearance of a wheal and/or erythema, the sign of a positive immediate skin reaction. The skin test was done thirty minutes preceding myelography and in over 40 cases no positive reactions were observed. More

recently, however, 2 cases have been seen presenting delayed meningeal reactions accompanied by flare-ups at the original skin test sites.

### CASE HISTORIES

CASE 1: A 22-year-old male was admitted to the hospital because of atrophy of the left lower extremity, of some five years duration, associated with persistent aching pain for the past year. The family history was essentially negative. The past history failed to reveal any episodes suggestive of poliomyelitis. The patient, had, however, suffered annual attacks of ragweed hay fever. The physical examination disclosed generalized weakness in the atrophic muscles, but no adventitious movement. The deep tendon reflexes were equal except for the left Achilles, which was absent. There were no sensory disturbances. Cerebrospinal fluid studies were within normal limits. It was felt that this patient probably had had unrecognized poliomyelitis, with his present complaints originating from a postural imbalance associated with the atrophy. A myelogram was deemed advisable, however, in order to complete the data.

An intracutaneous skin test with 0.1 ml. of pantopaque was done with no immediate local reaction, and 6 ml. of pantopaque was introduced intrathecally one-half hour later. No significant abnormalities were noted and the major portion of the medium was removed at the completion of the examination. A post-myelography lumbar film revealed a few globules of pantopaque remaining in the cul-de-sac. There was no febrile reaction or other immediate evidence of disturbance from the myelographic procedure.

On the ninth day following myelography the patient complained of pain and swelling of the arm at the site of the earlier pantopaque skin test. Examination revealed a raised, purplish-red, painful, indurated lesion, 4 cm. in diameter, involving the skin but with no evidence of purulent inflammation. On the tenth day there was increased local pain at the injection site, with generalized malaise and a low-grade febrile response. Twelve hours later severe headache and chills developed and the temperature

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rose to 102° F. General and neurological examinations at this time revealed moderate nuchal rigidity, generalized irritability, and photophobia, but no other significant findings. On the eleventh day there was a marked increase in the signs of meningitis, with the onset of nausea, vomiting, and mental confusion. A lumbar puncture revealed turbid fluid containing 370 red blood cells and 707 white blood cells per cubic millimeter, 507 being polymorphonuclear cells. The peripheral white blood cell count was 18,950 with 65 per cent segmented cells (1 juvenile, 1 band cell), 29 per cent lymphocytes, 2 per cent eosinophils, 1 per cent basophils, and 3 per cent monocytes. A second lumbar puncture was performed with no essential change in the cell count, but the protein was 113 mg. per cent. A Gram stain on this fluid revealed no organisms, and repeated cultures proved to be negative. By the following morning, the twelfth day, the patient was semistuporous, with a temperature of 101° F., marked nuchal rigidity, positive Kernig's sign, and absence of the left patellar reflex. Clinical improvement followed during the next twenty-four hours, with a return of consciousness, normal temperature, and marked remission of the signs of meningeal irritation. The skin reaction on the left forearm was less pronounced, and no significant adenopathy was noted. The next day—four days after the first symptoms—all clinical and laboratory signs were normal and remained so thereafter.

The sequence of events observed in this case led to the supposition that pantopaque hypersensitivity could have been the etiological factor. Further investigation yielded the following data: Routine scratch and intradermal skin tests to the common foods, dusts, molds, and pollens showed positive reactions only to grasses and to ragweed. Passive transfer tests (Prausnitz-Kustner), although positive for ragweed, were inconclusive for pantopaque. Scratch tests were negative for pantopaque. An intradermal test, using 0.1 ml. of pantopaque, was followed by the gradual development of an immediate positive skin reaction, consisting of a wheal and an area of erythema which reached a 4 cm. diameter within one hour. During the next hour, the central raised area increased to a diameter of 2 cm., and 2 pseudopods developed. The reaction subsided within two and a half hours, followed by a persistent area of erythema approximately 4 cm. in diameter, which had an appearance compatible with a delayed type of reaction such as is seen in some positive bacterial antigen reactions. The acute inflammatory reaction persisted for a period of five days and then slowly faded during the following six days, leaving a dull salmon-colored area of wrinkled skin 1.5 cm. in diameter. This discoloration persisted for two weeks and then slowly disappeared. At no time following this second introduction of pantopaque intracutaneously were there any evidences whatsoever of systemic reaction or of recurrence of meningeal irritation.

**CASE 2:** A 22-year-old white male was admitted to the hospital complaining of severe low back pain of twenty-four hours duration with radiation into the distribution of the right sciatic nerve. He was unable to walk without a marked list to the left. Pain was increased by coughing and sneezing. Occasional tingling paresthesias were noted in the right foot.

The family history was essentially negative. The past history revealed an acute illness at the age of six which was stated to have been poliomyelitis; no muscular or skeletal sequelae followed this illness. There was a positive history of annual ragweed hay fever. Roentgenograms revealed evidence of narrowing of the L5-S1 interspace. The routine laboratory work, including cerebrospinal fluid studies, was within normal limits. A trial of traction was only moderately successful in relieving pain.

Two weeks after admission, lumbar myelography was undertaken. A preliminary skin test was made, 0.1 ml. of pantopaque being injected intracutaneously, on the right forearm, with no immediate reaction. Thirty minutes later 6 ml. of pantopaque were introduced intrathecally, demonstrating a defect at the 5th lumbar interspace on the right.

At the completion of the examination, the patient was returned to the ward without removal of the opaque medium. The following morning, under fluoroscopic control, the major portion of the pantopaque was removed. X-ray studies of the entire spinal axis and posterior fossa revealed a few globules of pantopaque remaining in the caudal sac and in the basal cistern. The temperature rose to 101° in the next twenty-four hours, with associated headache, but with no other signs of meningeal irritation. It returned to normal within forty-eight hours of myelography and remained normal for one month. The patient refused surgical treatment and therefore was placed in continuous traction for a period of two weeks, followed by gradual ambulation. The pain in the back and right lower extremity subsided slowly.

Thirty days after myelography, the patient complained of irritability, headache, and pain in the neck and low back. The site of the pantopaque skin test was also painful and tender. On questioning, the patient stated that he had noticed the change at the skin test site one day previously. Examination revealed a raised purplish-red indurated lesion approximately 2 cm. in diameter involving the skin of the forearm; there was no evidence of purulent inflammation or of lymphangitis. There was nuchal rigidity but no signs of neurological disturbances other than those ascribed to nerve root compression. Within twenty-four hours the temperature had subsided from a maximum of 102° to normal and the signs of meningeal irritation had cleared completely within forty-eight hours of onset. No lumbar puncture was performed at this time. No antibiotic therapy was administered. The skin reaction subsided slowly over a period of one week.



Seven months after the sequence of events recorded above, the patient was studied in a manner similar to that described in Case 1. Routine scratch and intradermal skin tests to the common foods, dusts, molds, and pollens showed positive reactions only to grasses and to ragweed. Passive transfer tests (Prausnitz-Kustner) were again positive for ragweed but inconclusive for pantopaque. Pantopaque scratch tests were negative. An intradermal test with 0.1 ml. of pantopaque was followed by no immediate reaction. There was no visible or palpable evidence of change for a period of seven days. At the end of that period a slightly indurated, elevated area became palpable at the site of the intradermal test; the induration measured 1 cm. in diameter, was non-tender, and was associated with a very slight reddish discoloration of the skin. There were no systemic symptoms or signs. There was an increase in the indurated area to a diameter of 1.5 cm. during the next two days and then a gradual subsidence of all local signs in the ensuing five days.

A review of the two cases reported above reveals the following pertinent points:

(1) The original intradermal test with pantopaque did not give an immediate reaction in either instance.

(2) Small amounts of residual pantopaque were visualized in the subarachnoid space in each instance following removal of the major portion of the medium after myelography.

(3) Nine days following the skin test and myelography in one case and thirty days after these procedures in the other, flare-ups were observed at the sites of the original intradermal tests.

(4) Signs of acute meningitis developed, roughly coincident with the flare-up of the skin reaction in both cases.

(5) Cerebrospinal fluid studies in Case 1 revealed increased protein, with an inflammatory cellular type of response but with repeated negative cultures for infectious organisms. No lumbar puncture was performed in Case 2 at the time of the mild and transient meningeal symptoms.

(6) Each case showed a rapid subsidence of symptoms of meningitis with a parallel but slower subsidence of the skin reaction.

(7) Both patients gave histories of seasonal ragweed hay fever and positive reactions to ragweed, both on skin tests and passive transfer tests.

(8) Markedly positive immediate and

delayed skin reactions to intradermal retesting with pantopaque were elicited in the first case. Similar retesting in the second case showed no immediate reaction but was followed by a positive delayed skin test.

#### DISCUSSION

The reactions here reported do not correspond with the characteristic picture of the Schwartzman phenomenon (4). It would appear that in the two cases described, a specific hypersensitivity to pantopaque was produced either by the small intradermal injection or by the intrathecal introduction of this material or by both. In view of the fact that delayed meningeal reactions of this type have not been observed following myelography alone, the preliminary skin test may be considered the sensitizing agent. Similar sensitization, as well as the flare-up phenomenon following single small intradermal injections of foreign material, have been noted in man (5-7) and in experimental animals (8, 9). Such reactions have almost invariably been of the delayed type. Of the two subjects of this report, one clearly showed both types of reaction, while the other appeared to have only a delayed type. Nothing in the character of the meningeal reaction makes possible a distinction between the two. The presence of atopic allergy in both patients, as demonstrated by positive histories of seasonal ragweed hay fever and positive ragweed skin and passive transfer tests, may possibly be coincidental, since such a condition is not necessary for the production of sensitization of the type described (5-9).

Since the skin test with pantopaque has not been shown to have any usefulness in preventing the commoner type of reaction to myelography and since in occasional individuals it appears to be an effective sensitizer, its use in association with myelography appears to be contraindicated.

#### SUMMARY

(1) Two cases have been reported showing evidence of non-infectious meningitis



following the use of pantopaque for myelography after intradermal skin testing with the same material.

(2) Both patients gave a personal history of atopic ragweed hay fever, confirmed by positive ragweed skin and passive transfer tests.

(3) The delayed appearance of non-infectious meningitis has not been observed in a large series of cases submitted to pantopaque myelography in the absence of previous intradermal testing.

(4) These positive skin reactions to pantopaque are considered to be compatible with reactions both of the immediate type and of the delayed type observed in the field of allergy.

(5) Concomitant use of pantopaque for skin testing and for myelography is contraindicated.

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#### SUMARIO

##### Meningitis Debida a Hipersensibilidad al Pantopaco

Los 2 casos comunicados son de meningitis no infecciosa consecutiva al empleo de pantopaco para la mielografía, después de resultar negativas las cutirreacciones ejecutadas con la misma substancia. En ambos casos, visualizáronse pequeños residuos de pantopaco en el espacio subaracnoideo después de retirar la mayor parte del medio a continuación de la mielografía. A los nueve días de la prueba primitiva en un caso, y a los treinta en el otro, aparecieron signos de meningitis aguda asociados a una reacción en el sitio de la primitiva cutirreacción. Ambos revelaron rápida aten-

nuación de los síntomas de meningitis con una atenuación paralela, pero más lenta, de la reacción cutánea. Ambos enfermos comunicaron antecedentes de polinosis estacional por *Ambrosia artemisiaeflora*.

Como no se ha observado aparición tardía de meningitis no infecciosa en una numerosa serie de casos en que se ejecutó la mielografía con pantopaco sin previas cutirreacciones, parece que la inyección preliminar del medio en cuestión obró como sensibilizador en dichos casos. Opínase, pues, que esa comprobación preliminar está contraindicada.

# An Adaptometer for Preparation for Fluoroscopy<sup>1</sup>

FRANK A. RIEBEL, M.D., and C. C. CARROLL<sup>2</sup>

EVERY FLUOROSCOPIST has a method of determining when his eyes are dark-adapted; he wears goggles for a timed period, gauges his eyes by a light leak in the room, or perhaps switches the tube on and off until satisfied. Presented here is a low brightness adaptometer which will take the guess out of this chore. It consists of five self-luminous segments which are recessed into a rotating back plate. The luminosity is provided by phosphors excited by the beta radiation from the radioisotope, strontium<sup>90</sup>,<sup>3</sup> and the inserts have the following surface brightnesses:

No. 1.....	0.60 microlambert
No. 2.....	0.025 microlambert
No. 3.....	0.0105 microlambert
No. 4.....	0.0048 microlambert
No. 5.....	0.0026 microlambert

A brighter red fixation point is located just above the window through which the luminous disks are exposed. The shutter is so situated that the fixation point is covered, or partly covered, as desired, when the window is open.

The disks exhibit a certain degree of phosphorescence: accordingly the shutter should be kept closed in bright light. If exposure accidentally occurs, a 12-hour period should be allowed before use; otherwise spurious results will be obtained.

The time required by six different observers to adapt to the various disks was as follows:

Observer	No. 1	No. 2	No. 3	No. 4	No. 5
F. R.	5'	7 <sup>1</sup> / <sub>2</sub> '	11'	13'15"	15'30"
I. M.	50"	3'10"	4'50"	8'50"	11'10"
J. E.	9'50"	12'30"	16 <sup>1</sup> / <sub>2</sub> '	20'	22'30"
V. R.	1'	1'30"	4'30"	8'45"	13'30"
M. G.	2'	6'	15'	26'	38'
J. M.	2'50"	5'40"	8'50"	....	....

In all the above readings the observers had previously been in sunlit interiors. Observer J. M. was red-green color-blind and

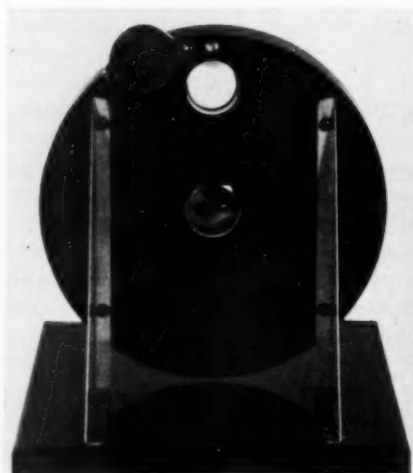


Fig. 1. Adaptometer: window open.

wore correction lenses for myopia and astigmatism. Although with these he had 20/20 vision, he was unable to see disks 4 and 5.

The variations among individuals exhibited here indicate the error in undergoing adaptation by the clock. This is further pointed up by the following readings in a single day by one observer who was exposed to various lightings before entering the darkroom.

Condition	No. 1	No. 2	No. 3	No. 4	No. 5
Daylight					
Interior	5'	7'30"	11'	13'30"	15'30"
Night					
Bright					
interior	1'5"	1'35"	4'55"	8'10"	13'5"
Dim					
interior	15"	30"	50"	1'50"	5'50"

The instrument is essentially free from radiation hazard, there being no detectable reading when an exposed ionization chamber (Victoreen, low scale to 2.5 mr. per hour) was juxtaposed to the luminous sealed-in disks.

<sup>1</sup> Accepted for publication in April 1951.

<sup>2</sup> Chief Chemist, U. S. Radium Corporation, Bloomsburg, Penna.

<sup>3</sup> The radioisotope was obtained from Oak Ridge National Laboratory, and the equipment was fabricated in the Laboratories of the United States Radium Corporation.

*Note:* Since submission of this article we have found it advisable to use  $C^{14}$  instead of  $St^{90}$  in the phosphors, because of the longer half-life.

Also developed is a smaller adaptometer

containing two self-luminous segments only, and suitable for attachment to the fluoroscopic screen mount.

15 W. Goodale St.  
Columbus, Ohio

#### SUMARIO

##### Adaptómetro para la Preparación para la Roentgenoscopia

El adaptómetro descrito está destinado para la adaptación a la oscuridad, como preliminar de la fluoroscopia. Consta de cinco segmentos autoluminosos de varios grados de brillantez superficial que se esconden en una placa rotatoria atrás. Un punto rojo más brillante de fijación está situado precisamente encima de la venta-

nilla por la que asoman los discos luminosos. Hay además un obturador situado de tal modo que cubre del todo o en parte, según se desee, el punto de fijación, al abrir la ventanilla. El distinto tiempo que requiere para adaptación cada observador denota la necesidad que hay de un indicador de este género.



## A New Radiolaryngometric Method<sup>1</sup>

DR. C. E. GÁRCIGA

Radium Institute, Havana, Cuba

A SIMPLE DEVICE of our own design has proved useful in conjunction with a lateral roentgenogram of the larynx for locating certain areas in the laryngeal region. This permits more direct irradiation of laryngeal lesions over the smallest possible area in relation to the extent of involvement.

The apparatus is merely a square made

ruler and the square. The roentgenogram is then taken in profile position (Fig. 3). After exposure and development of the film, the location of the lesion is determined in relation to the pencil marks previously made on the skin (Fig. 4). The area is then marked with a 10 per cent solution of silver nitrate to limit the area of irradiation (Fig. 5).

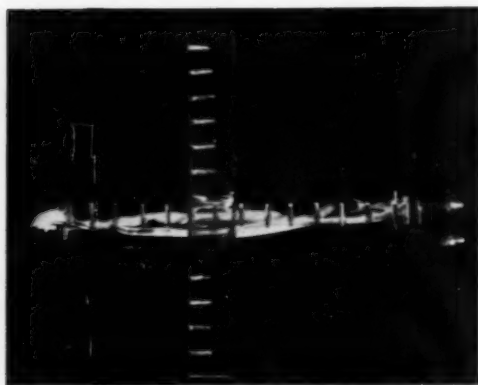


Fig. 1. Plastic square and sliding ruler.



Fig. 2. Device tied in place with ribbons.

of plastic material (lucite) which is radio-transparent. Over one of its bars a ruler slides from side to side. Embedded in the main branch of the square and in the sliding ruler are fine lead lines at intervals of 1 cm. (Fig. 1).

The square is tied to the neck by means of ribbons fastened to the ends of the branches and is fixed over the side to be treated, up to the height of the inferior border of the thyroid cartilage. The ruler (in vertical position) is moved until it coincides with the anterior border of the vertical axis of the larynx (Fig. 2). With the device so fixed, dots are marked with a dermatographic pencil on the skin, corresponding with the lead marks or lines on the



Fig. 3. Patient in position for roentgenography. The pencil markings on the skin correspond with the lead lines of the square and ruler. The plastic square should be put in position again before the exposure.

<sup>1</sup> Read before the Sixth International Congress of Radiology, London, England, July 1950. Accepted for publication in March 1951.





Fig. 4. Roentgenogram showing relation of lesion to the skin markings.



Fig. 5. Area of irradiation marked with silver nitrate solution.

#### SUMARIO

##### Nuevo Método Radiolaringométrico

Un sencillo aparatito diseñado por el A. ha resultado útil, en unión de una radiografía lateral de la laringe, para localizar ciertas zonas de dicha región. Esto permite la irradiación más directa de las lesiones laríngeas en la zona más pequeña posible en relación con la proporción de tejido afectado.

El aparato consiste meramente en un cuadrado hecho de una substancia plástica (lucita) que es radiotransparente, sobre una de cuyas barras se desliza una regla de lado a lado. Incrustadas en la rama principal del cuadrado y en la regla corrediza van, a espacios de 1 cm., finas líneas de plomo.

El cuadrado se sujeta al cuello por medio de cintas amarradas a los extremos de las

barras y se fija sobre el lado por tratar, hasta la altura del borde inferior del cartílago tiroideo. La regla (en posición vertical) es movida hasta que coincida con el borde anterior del eje vertical de la laringe. Ya fijo así el accesorio, se trazan con un lápiz dermatográfico puntos en la piel, que corresponden a las marcas o líneas de plomo que aparecen en la regla y el cuadrado. Luego se toma la radiografía en perfil. Después de la exposición y revelado de la película, se determina la localización de la lesión en relación con las marcas hechas anteriormente con el lápiz en la piel. La zona se marca luego con solución de nitrato de plata al 10 por ciento para delimitar la zona de irradiación.

# EDITORIAL

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## Radiation Protection During Diagnostic Studies

With the present widespread use of radiologic methods of diagnosis by both trained and untrained personnel, the problem of protection from direct and stray radiation has assumed increasing importance. In the case of the operator, the danger may lie in exposure to stray radiation over a long period of time or in injudicious exposure to direct radiation as a result of inadequate shielding or disregard of safety factors. The patient may be unwittingly over-irradiated because of poor judgment on the part of the radiologist or may suffer from the cumulative effect of successive examinations when a full history of earlier exposure has been withheld.

Fluoroscopy is probably attended by the greatest danger unless adequate precautions are taken. Braestrup showed by measurement studies that increasing the target-panel distance from 8 to 12 inches reduced the skin dose about 33 per cent with the same  $r$  per minute at the screen. Decreases in the dose to the skin were shown to be obtainable, also, by an increase in the added filtration, a reduction of 50 per cent being accomplished by an additional 0.5 to 1.0 Al without any loss in the diagnostic value of the image. Smaller fields not only cut down the area of exposure but also reduced back-scatter and, finally, with higher voltage the skin dose was less for the same illumination.

It was also found by Braestrup that the fluoroscopist may be the recipient of appreciable amounts of stray radiation when using a fluoroscope of the horizontal or tilt type, because of the space left between the shielding cone and the table top to permit movement of the Bucky diaphragm. This scattering is of much greater intensity than scattered radiation from the patient. The danger can be mitigated, however, by

adequate shielding of the open space, although protective gloves and apron or a lead-protected chair are still highly essential. After ascertaining the number of  $r$  per minute received by the patient's skin on any given installation, a self-limiting fluoroscopic timer will add an excellent safety factor.

In routine radiography there is little reason for the operator to receive any appreciable dose of radiation if the control is properly located and shielded, and if he exercises the basic rules of safety. Certain radiographic procedures, however, may entail excessive exposure unless special precautions are observed. The examination of infants and small children falls within this category, since often the child must be held by an attendant. This should be someone not regularly exposed to radiation, or a protective lead-rubber apron and gloves should be worn. Under no circumstances should an x-ray technician or operator hold dental films in the patient's mouth while an exposure is being made, as this will inevitably lead to severe radiation damage. Roentgen studies of the mentally defective also present a special problem, as these patients must frequently be held in position. Heustis and Van Farowe in a paper in this issue of *RADIOLOGY* review the problem as they have observed it in mental institutions in Michigan. Many of the measures which they suggest to correct the conditions encountered in their survey are equally applicable to x-ray installations elsewhere.

In the various angiographic procedures which are becoming increasingly popular, there are inherent dangers both to the radiographer and to the clinician unless adequate protective measures are adopted. The multiple exposures of high intensity

must rightly cause apprehension. A similar risk of over-exposure to secondary radiation is entailed in retrograde urethro-cystography, in which injection of the contrast medium must be made while the exposure is in progress if the prostatic portion of the urethra is to be visualized.

Two of the greatest hazards, both to the radiologist and the surgeon, are the setting of fractures and the removal of foreign bodies from the soft tissues under fluoroscopic control. Either procedure is difficult or impossible when rayproof gloves are worn. It is of the first importance, therefore, that the hands be kept out of the field during the time the image is being viewed. The hands of many radiologists and surgeons bear mute testimony to the breaking of this rule.

In recent years there has been a growing concern over the skin dosage received by the patient during routine radiographic examination. Smedal made a study of this problem showing that with unfiltered radiation certain multiple-film studies produced a near-erythema dose. He found that in examinations of the urinary tract a 1.0-mm. aluminum filter reduced the skin dose markedly while causing little change in the film effect for the same tube factors. The depth dose received in pelvimetry studies he considered negligible and unimportant. Martin also showed the beneficial effects of 1.0 mm. aluminum filtration, as well as of increasing the focal-skin distance.

That persons engaged in handling radioactive materials, or otherwise exposed to radiation in the course of their work, run an added risk when submitted to roentgen examination is pointed out by Handloeser and Love of the Brookhaven National Laboratories. In their study of this problem they have constructed a table setting forth the exposures incident to the more common diagnostic procedures.

A simple method whereby skin dosage may be quickly computed was devised by Sorrentino and Yalow. A nomogram which they constructed for this purpose was found to be accurate to within  $\pm 25$  per

cent. In an investigation of seven machines they found the x-ray output per milliampere second in all cases to be within  $\pm 10$  per cent of the average.

In connection with the general problem of protection, attention is directed to the National Bureau of Standards Handbook 41, which should be in the possession of every radiologist. This outlines the safety measures necessary for protection against radiation up to two million volts, as well as against the electrical hazards involved. The radiologist should also familiarize himself with the International Recommendations on Radiological Protection as revised by the International Commission on Radiological Protection at the Sixth International Congress of Radiology in 1950 and published in RADIOLOGY for March 1951.

Radiation protection may seem to be an old story, and many of the observations made here will appear trite, but we cannot afford to be complacent in face of the dangers to which both the operator and the patient are exposed when the rules of safety are ignored. In the final analysis the radiologist must bear the responsibility. He must be cognizant of the risks inherent in his specialty. He must provide equipment which makes protection possible and see that it is used. He must make sure that safety rules are enforced. Finally, he must himself set the example of respect for the agent with which he works and its potentialities for harm as well as good.

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## ANNOUNCEMENTS AND BOOK REVIEWS

### MISSISSIPPI RADIOLOGICAL SOCIETY

The most recent addition to the roster of State radiological groups is the Mississippi Radiological Society. The new society meets the third Thursday of each month at the Rotisserie Restaurant, Jackson. The secretary is John W. Evans, M.D., 621 High St., Jackson 2.

### OHIO STATE RADIOLOGICAL SOCIETY

At the annual convention of the Ohio State Radiological Society, held in Columbus, the following officers were elected: Donald D. Brannan, M.D., Cleveland, President; Edward C. Elsey, M.D., Cincinnati, Vice-President; Willis S. Peck, M.D., 2001 Collingwood Ave., Toledo, Secretary-Treasurer.

### SYMPOSIUM NEURORADIOLOGICUM

Announcement has been made of the third Symposium Neuroradiologicum to be held in Stockholm Sept. 17-20, 1952, under the presidency of Prof. Erik Lindgren. The main themes of the meeting will be Vertebral Angiography, Roentgen Diagnosis of Spinal Tumors, and Phlebography in Neuroradiology, though papers will also be presented on other neuroradiological subjects. A detailed program will appear early in 1952, and arrangements for hotel accommodations will be announced in due course. The subscription fee will be approximately Sw. Kr. 75:—for active members and Sw. Kr. 25:—for companions. Further details may be obtained by addressing Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K, Sweden.

### GRANTS AND FELLOWSHIPS IN RADIOLOGICAL RESEARCH

On behalf of the James Picker Foundation, the National Research Council announces the continued availability of Fellowships and Grants in Radiological Research.

*Fellowships in Radiological Research* offer research training for recent graduates entering upon investigative careers in the field. Stipends vary from \$3,000 to \$5,000 per annum, depending on the qualifications and special circumstances of the applicant. Candidates must have the M.D. or Ph.D. degree or equivalent experience and achievement in research. Appointments are not limited to citizens of the United States. Applications for 1952-53 must be postmarked on or before December 15, 1951.

*Grants in Radiological Research* are designed to encourage research leading to improvement in medical diagnosis and treatment oriented toward radiological methods. The Foundation has specifically requested that none of its funds be used to subsidize

the development of radiological equipment. Grants are not restricted to institutions within the United States. Applications for grants for the fiscal year 1952-53 must be postmarked on or before January 1, 1952.

Complete details and application blanks for Fellowships and Grants may be obtained from the Secretary, Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, N. W., Washington 25, D. C.

### EFFECT OF X-RAYS ON BACTERIA

An extensive bibliography on "The Effect of X-Rays on Bacteria" has been prepared by members of the research staff at Battelle Memorial Institute, Columbus, Ohio, and 500 copies have been printed for complimentary distribution. This subject is of considerable interest at the present time, as indicated by recent developments in radiation sterilization and the extensive research being done on the use of radioactive wastes for that purpose. The bibliography is available on request to Battelle Memorial Institute, 505 King Ave., Columbus 1, Ohio.

### ERRATUM

Attention is called to an unfortunate transposition of lines on page 190 of the August 1951 issue of *RADIOLOGY*, in the paper by Lange and Ødegaard on "Abrodil Myelography in Herniated Disk in the Lumbar Region." The first line in column 1, "the exact site of the lesion..." properly belongs at the foot of the column.

## Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

### AN ATLAS OF NORMAL RADIOGRAPHIC ANATOMY.

By ISADORE MESCHAN, M.A., M.D., Professor and Head of the Department of Radiology, University of Arkansas School of Medicine, with the Assistance of R. M. F. Farrer-Meschan, M.B., B.S. (Melbourne, Australia). A volume of 594 pages, with 362 figures comprising 1,044 illustrations. Published by W. B. Saunders Co., Philadelphia, Penna., 1951. Price \$15.00.

### CLINICAL LABORATORY DIAGNOSIS. By SAMUEL A.

LEVINSON, M.S., M.D., Ph.D., Director of Laboratories, University of Illinois Research and Educational Hospitals, Chicago, Ill.; Professor of Pathology, University of Illinois College of Medi-



cine, and ROBERT P. MACFATE, Ch.E., M.S., Ph.D., Chief, Bureau of Laboratories, Department of Health, City of Chicago; Assistant Professor of Pathology, University of Illinois College of Medicine; Formerly Assistant Director of Laboratories, University of Illinois Research and Educational Hospitals, Chicago, Ill. A volume of 1,146 pages, with 221 illustrations and 13 plates, 10 in color. Published by Lea & Febiger, Philadelphia, Penna., 4th ed., 1951. Price \$12.00.

**PRACTICAL ELECTRON MICROSCOPY.** V. E. COSSLETT, M.A., M.Sc., Ph.D., University Lecturer in Physics, Cavendish Laboratory, Cambridge, England. A volume of 300 pages, with 147 illustrations. Published by Academic Press, Inc., New York, and Butterworths Scientific Publications, London, 1951. Price \$5.50.

**INDUSTRIAL USES OF RADIOACTIVE FISSION PRODUCTS. A REPORT TO THE UNITED STATES ATOMIC ENERGY COMMISSION, SRI PROJECT NO. 361.** A monograph of 102 pages, with 26 illustrations. Published by the Stanford Research Institute, Stanford, Calif. Price \$1.50.

## Book Reviews

**A TEXT-BOOK OF X-RAY DIAGNOSIS.** By British Authors. In four volumes. Edited by S. COCHRANE SHANKS, M.D., F.R.C.P., F.F.R., Director, X-Ray Diagnostic Department, University College Hospital, London, and PETER KERLEY, M.D., F.R.C.P., F.F.R., D.M.R.E., Director, X-Ray Department, Westminster Hospital; Radiologist, Royal Chest Hospital, London. Vol. I. The Head and Neck. A volume of 434 pages, with 439 illustrations. Price \$12.00. Vol. II. Chest. A volume of 702 pages, with 605 illustrations. Published by W. B. Saunders Co., Philadelphia, 2d ed., 1951. Price \$15.00.

Volumes I and II of the second edition of the well known text on diagnostic radiology by British authors have appeared following Volumes III and IV, previously reviewed in this Journal, completing the work.

Volume I, on the Head and Neck, is divided into 5 parts, dealing with the central nervous system, the teeth and jaws, the eye, the accessory nasal sinuses, and the temporal bone. Each major subject is approached by consideration of anatomy, physiology, radiographic technic (when indicated by special problems), normal radiographic anatomy, and radiological interpretation. The study of each disease entity includes well emphasized clinical, pathological, and radiological correlation rather than mere descriptive radiology.

Of particular interest is the well written section on the Teeth and Jaws, a subject which has been somewhat neglected in the field of diagnostic radiology.

While much of the responsibility for interpretation of dental films lies with the dental surgeon, this section will be most valuable in bridging the gap between studies of the teeth and the jaws, which after all is more apparent than real. A subsection of the division is a chapter on Cysts and Tumors of the Teeth and Jaws. This subject is well covered, the very brevity of the chapter being in large part responsible for its clarity.

The last part of the book, The Radiology of the Temporal Bone, offers a comprehensive integration of anatomy, physiology, pathology, and radiographic interpretation of diseases of this complex area of the skull. Chief emphasis is upon diseases of the middle ear and mastoids, and their complications. This section will prove of interest to all students of radiology.

Volume II, on the Chest, is divided into two parts, devoted respectively to the cardiovascular system and the respiratory system. The section on the cardiovascular system includes individual chapters on the heart, aorta, pericardium, the pulmonary vessels, and the peripheral vessels. Only brief mention of the technic of roentgenkymography is made. The section would be improved by a more thorough discussion of this subject.

The second part of this volume presents the usual aspects of bronchopulmonary radiology in a thorough fashion. Well illustrated material is offered in the discussion of the bronchopulmonary segments. Individual chapters are devoted to the normal appearance and diseases of the diaphragm and the pleura.

Throughout the entire volume well advised stress is placed upon clinical correlation and radiological interpretation. This is particularly exemplified by a chapter discussing the postoperative appearance of the lungs. It is this sort of treatment which makes the series a comprehensive and valuable survey of the field of diagnostic radiology.

**ROENTGEN MANIFESTATIONS OF PANCREATIC DISEASE.** By MAXWELL HERBERT POPPEL, M.D., F.A.C.R., Associate Professor of Clinical Radiology, New York University-Bellevue Medical Center; Associate Roentgenologist, New York University Hospital; Associate Radiologist, Mount Sinai Hospital; Roentgenologist, Welfare Island Dispensary, New York City; Consultant in Radiology, United States Naval Hospital, St. Albans, Long Island, N. Y.; Attending Consultant in Radiology, United States Veterans Administration Hospital, Bronx, N.Y.; Commander (Medical Corps), United States Naval Reserve. A volume of 390 pages, with 166 illustrations. Published by Charles C Thomas, Springfield, Ill., 1951. Price \$10.50.

This book considers the pancreas and its relationship to other organs of the body as demonstrated roentgenologically and affords convincing evidence that many lesions of the pancreas may be deduced



through proper and careful examination of the various structures which surround it. Chapters on the development and anatomy of the pancreas and the duodenum and their congenital variations precede a chapter on roentgen methods, which in turn is followed by consideration of various pathological conditions.

Calcareous diseases of the pancreas, primary tumors, infections, exocrine deficiencies, and lesions secondary to disease elsewhere in the body are completely and clearly discussed. A final chapter gives the salient features in differential diagnosis of the various lesions of the pancreas which are demonstrable roentgenographically, either directly or indirectly.

The work is generously illustrated by roentgenograms, and tables of statistics and an extensive bibliography are included.

**THE MANAGEMENT OF FRACTURES, DISLOCATIONS, AND SPRAINS.** BY JOHN ALBERT KEY, B.S., M.D., St. Louis, Mo., Clinical Professor of Orthopedic Surgery, Washington University School of Medicine; Associate Surgeon, Barnes, Children's, and Jewish Hospitals, and H. EARLE CONWELL, M.D., F.A.C.S., Birmingham, Ala., Associate Professor of Orthopedic Surgery, University of Alabama School of Medicine; Chief of the Orthopedic Service, South Highland Infirmary; Consulting Orthopedic Surgeon to Carraway Methodist Hospital and Baptist Hospitals; Attending Orthopedic Surgeon, Children's Hospital, Jefferson-Hillman Hospital, East End Memorial Hospital, and St. Vincent's Hospital, Birmingham, Ala. A volume of 1,232 pages, with 1,195 illustrations. Published by C. V. Mosby Company, St. Louis, Mo., 5th ed., 1951. Price \$16.00.

In this new fifth edition of their text on Fractures, Dislocations, and Sprains, the authors present again a comprehensive—almost an exhaustive—treatise on injuries of the musculoskeletal system. The text is well arranged and readable. The index is unusually complete, which makes for easy reference.

Of special note are two aspects of the work: (1) the numerous and extraordinarily clear roentgenographic reproductions representing each type of condition and (2) the detailed descriptions and illustrations of the apparatus and appliances, including beds, plaster casts, and methods of traction, used in the treatment of fractures. This information, so essential to both the student and specialist, is rarely available in organized form. Here it is exceptionally complete.

This book is an epitome of extremes—completeness of detail for the expert and obfuscation for the uninitiated. The authors state in their Preface that

"this book is written for the student, the general practitioner, and the surgeon." However, the experience of an able specialist in traumatology of the musculoskeletal system is sometimes required to interpret the complexity of the conditions discussed. The uninitiated—or the physician in general practice who may be called on to treat an occasional bone or joint injury—finds certain statements confusing, as, for example, the designation of Kocher's method as "the most efficient and least traumatizing method yet devised for the reduction of subcoracoid dislocations," having been thoroughly indoctrinated in medical school, and again by the teachings of the "specialty groups" in postgraduate refresher courses, that this type of manipulation is applicable only in special instances—if ever—and to be attempted only by the experienced.

With such reservations the book can be recommended as at once a text for the student and a work of reference for the specialist in bone and joint injuries. The radiologist, too, will find the numerous excellent reproductions of roentgenograms well worth his attention.

**MICRO-ARTERIOGRAPHY AND OTHER RADIOLOGICAL TECHNIQUES EMPLOYED IN BIOLOGICAL RESEARCH.** BY ALFRED E. BARCLAY, O.B.E., M.D., D. Sc. (Hon.) Oxon., D.Sc. (Hon.) Manchester, F.R.C.P., F.F.R., F.A.C.R., Honorary Radiologist to the Nuffield Institute for Medical Research, Oxford. A volume of 102 pages, with 46 illustrations. Published by Charles C Thomas, Springfield, Ill., 1951. Price \$6.75.

This is a fascinating monograph, by a master craftsman and scientist who opened up for us an entirely new method of investigation of the vascular system, revealing not only its gross anatomy but its physiologic action in the normal and abnormal state. In its pages the reader is introduced to the subject of microarteriography, and the technic, as it evolved in the author's experience. The material was prepared for publication late in his life when, as he states in the Preface, the dice were loaded against him both as regards time and energy, but little is lost from this circumstance. Indeed, one of the points which is made most emphatically came to be fully realized only in the author's last years: that in biological research, the radiologist, even though unacquainted with the detail of the problem, should be fully aware of its nature and one of the key members of the team.

This monograph is a necessity to anyone who is doing radiologic research, involving the basic sciences of anatomy, physiology, pathology and general biology. Many beautiful microradiographs of the kidney and stomach illustrate the text.

## RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

*Editor's Note:* Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

**RADIOLOGICAL SOCIETY OF NORTH AMERICA.** *Secretary-Treasurer*, Donald S. Childs, M.D., 713 E. Genesee St., Syracuse 2, N. Y.

**AMERICAN RADIUM SOCIETY.** *Secretary*, John E. Wirth, M.D., 635 Herkimer St., Pasadena 1, Calif.

**AMERICAN ROENTGEN RAY SOCIETY.** *Secretary*, Barton R. Young, M.D., Germantown Hospital, Philadelphia 44, Penna.

**AMERICAN COLLEGE OF RADIOLOGY.** *Exec. Secretary*, William C. Stronach, 20 N. Wacker Dr., Chicago 6.

**SECTION ON RADIOLOGY, A. M. A.** *Secretary*, Paul C. Hodges, M.D., 950 East 59th St., Chicago.

### Alabama

**ALABAMA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. A. Meadows, Jr., M.D., Medical Arts Bldg., Birmingham 5.

### Arizona

**ARIZONA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, R. Lee Foster, M.D., 507 Professional Bldg., Phoenix. Annual meeting with State Medical Association.

### Arkansas

**ARKANSAS RADIOLOGICAL SOCIETY.** *Secretary*, Fred Hames, M.D., Pine Bluff. Meets every three months and at meeting of State Medical Society.

### California

**CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY.** *Secretary*, Sydney F. Thomas, M.D., Palo Alto Clinic, Palo Alto.

**EAST BAY ROENTGEN SOCIETY.** *Secretary*, Dan Tucker, M.D., 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

**LOS ANGELES RADIOLOGICAL SOCIETY.** *Secretary*, Harold P. Tompkins, M.D., 658 South Westlake Ave. Meets monthly, second Wednesday, County Society Bldg.

**NORTHERN CALIFORNIA RADIOLOGICAL CLUB.** *Secretary*, G. A. Fricker, Sacramento Co. Hospital, Sacramento 17. Meets at dinner last Monday of September, November, January, March, and May.

**PACIFIC ROENTGEN SOCIETY.** *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually with State Medical Association.

**SAN DIEGO ROENTGEN SOCIETY.** *Secretary*, R. F. Niehaus, M.D., 1831 Fourth Ave., San Diego. Meets first Wednesday of each month.

**SAN FRANCISCO RADIOLOGICAL SOCIETY.** *Secretary*, I. J. Miller, M.D., 2680 Ocean Ave., San Francisco 27. Meets quarterly.

**SOUTH BAY RADIOLOGICAL SOCIETY.** *Secretary*, Ford Shepherd, M.D., 526 Soquel Ave., Santa Cruz. Meets monthly, second Wednesday.

**X-RAY STUDY CLUB OF SAN FRANCISCO.** *Secretary*, Merrell A. Sisson, M.D., 450 Sutter St., San Francisco 8. Meets third Thursday at 7:45 January to June at Stanford University Hospital, July to December at San Francisco Hospital.

### Colorado

**COLORADO RADIOLOGICAL SOCIETY.** *Secretary*, Wendell P. Stampfli, M.D., 1933 Pearl St., Denver. Meets monthly, third Friday, at University of Colorado Medical Center or Denver Athletic Club.

### Connecticut

**CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary*, Fred Zaff, M.D., 135 Whitney Ave., New Haven. Meets bimonthly, second Wednesday.

**CONNECTICUT VALLEY RADIOLOGICAL SOCIETY.** *Secretary*, Ellwood W. Godfrey, M.D., 1676 Boulevard, W. Hartford. Meets second Friday of October and April.

### District of Columbia

**RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY.** *Secretary*, U. V. Wilcox, M.D., 915 19th St., N.W., Washington 6. Meets third Thursday, January, March, May, and October, at 8:00 P.M., in Medical Society Library.

### Florida

**FLORIDA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Nelson T. Pearson, M.D., 1109 Huntington Bldg., Miami. Meets in April and in November.

**GREATER MIAMI RADIOLOGICAL SOCIETY.** *Secretary*, Theodore M. Berman, M.D., 350 Lincoln Road, Miami Beach. Meets monthly, last Wednesday, 8:00 P.M., Veterans Administration Bldg., Miami.

### Georgia

**ATLANTA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. Dudley King, M.D., 35 Linden Ave., N. E. Meets second Friday, September to May.

**GEORGIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Robert C. Pendergrass, M.D., Americus. Meets in November and with State Medical Association.

### Illinois

**CHICAGO ROENTGEN SOCIETY.** *Secretary*, Benjamin D. Braun, M.D., 6 N. Michigan Ave., Chicago 11. Meets at the University Club, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

**ILLINOIS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Stephen L. Casper, M.D., Physicians and Surgeons Clinic, Quincy.

**ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary*, Willard C. Smullen, M.D., St. Mary's Hospital, Decatur.

### Indiana

**INDIANA ROENTGEN SOCIETY.** *Secretary-Treasurer*, William M. Loehr, M.D., 712 Hume-Mansur Bldg., Indianapolis 4. Annual meeting in May.

### Iowa

**IOWA X-RAY CLUB.** *Secretary*, Arthur W. Erskine, M.D., 326 Higley Building, Cedar Rapids. Meets during annual session of State Medical Society.

**Kansas**

KANSAS RADIOLOGICAL SOCIETY. *Secretary*, Charles M. White, M.D., 3244 East Douglas, Wichita 8. Meets annually with State Medical Society.

**Kentucky**

KENTUCKY RADIOLOGICAL SOCIETY, *Secretary*, Everett L. Pirkey, M.D., Louisville General Hospital. Meets monthly, second Friday, at Seelbach Hotel.

**Louisiana**

LOUISIANA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Johnson R. Anderson, M.D., No. Louisiana Sanitarium, Shreveport. Meets with State Medical Society.

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets first Tuesday of each month.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday.

**Maine**

MAINE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Clark F. Miller, M.D., Central Maine General Hospital, Lewiston.

**Maryland**

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary-Treasurer*, Richard B. Hanchett, M.D., 705-6, Medical Arts Bldg., Baltimore 1. Meets third Tuesday, September to May.

**Michigan**

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary*, James C. Cook, M.D., Harper Hospital, Detroit 1. Meets first Thursday, October to May, at Wayne County Medical Society club rooms.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS. *Secretary-Treasurer*, R. B. MacDuff, M.D., 220 Genesee Bank Building, Flint 3.

**Minnesota**

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary*, Leo A. Nash, M.D., 572 Lowry Medical Arts Bldg., St. Paul 2. Meets in Spring and Fall.

**Missouri**

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, Wm. M. Kitchen, M.D., 1010 Rialto Building, Kansas City 6, Mo. Meets last Friday of each month.

ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary*, Donald S. Bottom, M.D., 510 S. Kingshighway Blvd. Meets on fourth Wednesday, October to May.

**Nebraska**

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Russell W. Blanchard, M.D., 1216 Medical Arts Bldg., Omaha. Meets fourth Thursday of each month at 6 P.M. in Omaha or Lincoln.

**New England**

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary*, L. L. Robbins, M.D., Massachusetts General Hospital, Boston 14. Meets monthly on third Friday at the Harvard Club, Boston.

**New Hampshire**

NEW HAMPSHIRE ROENTGEN SOCIETY. *Secretary*, Albert C. Johnston, M.D., Elliot Community Hospital, Keene. Meets quarterly in Concord.

**New Jersey**

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, Nicholas G. Demy, M.D., 912 Prospect Ave., Plainfield. Meets at Atlantic City at time of State Medical Society and midwinter in Elizabeth.

**New York**

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC. *Secretary*, William J. Francis, M.D., East Rockaway.

BROOKLYN ROENTGEN RAY SOCIETY. *Secretary*, J. Daversa, M.D., 603 Fourth Ave., Brooklyn. Meets fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meets second Monday, October to May.

CENTRAL NEW YORK ROENTGEN SOCIETY. *Secretary*, Dwight V. Needham, M.D., 608 E. Genesee St., Syracuse 10. Meets in January, May, October.

KINGS COUNTY RADIOLOGICAL SOCIETY. *Secretary*, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meets fourth Thursday, October to May, at 8:45 P.M., Kings County Medical Bldg.

NEW YORK ROENTGEN SOCIETY. *Secretary*, Irving Schwartz, 45 E. 66th St., New York 21.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John F. Roach, M.D., Albany Hospital, Albany. Meets at University Club, Albany, second Wednesday, October, November, and March. Annual Meeting in June to be announced.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary-Treasurer*, George Gamsu, M.D., 191 S. Goodman St. Meets at Strong Memorial Hospital, last Monday of each month, September through May.

**North Carolina**

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary*, James E. Hemphill, M.D., Professional Bldg., Charlotte 2. Meets in May and October.

**North Dakota**

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary*, P. H. Woutat, M.D., 322 Demers Ave., Grand Forks.

**Ohio**

OHIO STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Willis S. Peck, M.D., 2001 Collingwood Ave., Toledo. Meets with State Medical Association.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary*, Frank A. Riebel, M.D., 15 W. Goodale St., Columbus. Meets second Thursday, October, December, February, April, and June, 6:30 P.M., Columbus Athletic Club, Columbus.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mortimer Lubert, M.D., Heights Medical Center Bldg., Cleveland Heights 6. Meets at 6:45 P.M. on fourth Monday, October to April, inclusive.

**GREATER CINCINNATI RADIOLOGICAL SOCIETY.** *Secretary*, Lee S. Rosenberg, M.D., Jewish Hospital, Cincinnati 29. Meets first Monday, October through May.

**MIAMI VALLEY RADIOLOGICAL SOCIETY.** *Secretary*, Geo. A. Nicoll, M.D., Miami Valley Hospital, Dayton. Meets monthly, second Friday.

#### Oklahoma

**OKLAHOMA STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, W. E. Brown, M.D., 21st and Xanthus, Tulsa 4. Meets in October, January, and May.

#### Oregon

**OREGON RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. Richard Raines, M.D., Medical-Dental Bldg., Portland 5. Meets monthly, second Wednesday, October to June, at 8:00 P.M., University Club.

#### Pacific Northwest

**PACIFIC NORTHWEST RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Sydney J. Hawley, M.D., 1320 Madison St., Seattle 4. Meets annually in May.

#### Pennsylvania

**PENNSYLVANIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, James M. Converse, M.D., 416 Pine St., Williamsport 8. Meets annually.

**PHILADELPHIA ROENTGEN RAY SOCIETY.** *Secretary*, George P. Keefer, M.D., American Oncologic Hospital, Philadelphia 4. Meets first Thursday of each month at 8:00 P.M., from October to May, in Thomson Hall, College of Physicians.

**PITTSBURGH ROENTGEN SOCIETY.** *Secretary-Treasurer*, Edwin J. Euphrat, M.D., 3500 Fifth Ave., Pittsburgh 13. Meets monthly, second Wednesday, at 6:30 P.M., October to May, at Webster Hall.

#### Rocky Mountain States

**ROCKY MOUNTAIN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Maurice D. Frazer, M.D., 1037 Stuart Bldg., Lincoln, Nebr.

#### South Carolina

**SOUTH CAROLINA X-RAY SOCIETY.** *Secretary-Treasurer*, Henry E. Plenge, M.D., 855 N. Church St., Spartanburg. Meets with State Medical Association in May.

#### South Dakota

**RADIOLOGICAL SOCIETY OF SOUTH DAKOTA.** *Secretary-Treasurer*, Marianne Wallis, M.D., 1200 E. Fifth Ave., Mitchell. Meets with State Medical Society.

#### Tennessee

**MEMPHIS ROENTGEN CLUB.** *Secretary*, John E. White-leather, M.D., 899 Madison Ave. Meets first Monday of each month at John Gaston Hospital.

**TENNESSEE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meets annually with State Medical Society in April.

#### Texas

**DALLAS-FORT WORTH ROENTGEN STUDY CLUB.** *Secretary*, X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth 2. Meets monthly, third Monday, in Dallas odd months, Fort Worth even months.

**HOUSTON RADIOLOGICAL SOCIETY.** *Secretary*, Frank M. Windrow, M.D., 1205 Hermann Professional Bldg.

**TEXAS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, R. P. O'Bannon, M.D., 650 Fifth Ave., Fort Worth. Next meeting, Jan. 18-19, 1952, Houston.

#### Utah

**UTAH STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Angus K. Wilson, M.D., 343 S. Main St., Salt Lake City. Meets third Wednesday, January, March, May, September, November.

#### Virginia

**VIRGINIA RADIOLOGICAL SOCIETY.** *Secretary*, P. B. Parsons, M.D., Norfolk General Hospital, Norfolk.

#### Washington

**WASHINGTON STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, R. C. Kiltz, M.D., 705 Medical-Dental Bldg., Everett. Meets fourth Monday, October through May, at College Club, Seattle.

#### Wisconsin

**MILWAUKEE ROENTGEN RAY SOCIETY.** *Secretary-Treasurer*, Theodore J. Pfeffer, M.D., 839 N. Marshall St., Milwaukee 2. Meets monthly on second Monday at the University Club.

**RADIOLOGICAL SECTION OF THE WISCONSIN STATE MEDICAL SOCIETY.** *Secretary*, Abraham Melamed, M.D., 425 E. Wisconsin Ave., Milwaukee. Meets in May and with State Medical Society, September.

**UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE.** Meets first and third Thursdays 4 P.M., September to May, Service Memorial Institute.

**WISCONSIN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Irving I. Cowan, M.D., 425 East Wisconsin Ave., Milwaukee 2.

#### CANADA

**CANADIAN ASSOCIATION OF RADIOLOGISTS.** *Honorary Secretary-Treasurer*, Jean Bouchard, M.D. *Assoc. Hon. Secretary-Treasurer*, D. L. McRae, M.D. *Central Office*, 1555 Summerhill Ave., Montreal 26, Quebec. Meets in January and June.

**LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES.** *General Secretary*, Origène Dufresne, M.D., Institut du Radium, Montreal. Meets third Saturday each month.

#### CUBA

**SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA.** Offices in Hospital Mercedes, Havana. Meets monthly.

#### MEXICO

**SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA.** *General Secretary*, Dr. Dionisio Pérez Cosío, Marsella 11, Mexico, D. F. Meets first Monday of each month.

#### PANAMA

**SOCIEDAD RADIOLOGICA PANAMEÑA.** *Secretary-Editor*, Luis Arrieta Sánchez, M.D., Apartado No. 86, Panama, R. de P.

#### PUERTO RICO

**ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA.** *Secretary*, Jesús Rivera Otero, M.D., Box 3542 Santurce, Puerto Rico.



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## ROENTGEN DIAGNOSIS

### THE HEAD AND NECK

**Cerebral Angiography.** J. B. Curtis. *Brit. J. Surg.* 38: 295-331, January 1951.

The author reviews the historical development of cerebral angiography and describes the percutaneous technic (see Lindgren: *Brit. J. Radiol.* 20: 326, 1947. *Abst. in Radiology* 51: 123, 1948). Two complications of the procedure are discussed: perivascular hematoma and formation of a fibrinous clot in the lumen of the needle. The author avoids this latter occurrence by treating the needles with silicone (see Jaques *et al.*: *Canad. M.A.J.* 55: 26, 1946). Damage to the vessels is a third possibility but is believed to be rare.

Diodone is used as a contrast substance. As a rule, the amount should not exceed 60 c.c. of a 35 per cent solution. Its use in any amount is contraindicated in patients with renal damage, gross hypertension, or an allergic history.

The exact radiographic technic is described and the importance of correct positioning is stressed.

Over 700 carotid angiograms have been made in the Nuffield Department of Surgery, Oxford, and on the basis of these the appearances in the normal subject and in patients with intracranial tumors are described. Special stress is laid upon the variations of the normal pattern as seen in the lateral and anteroposterior projections, and these are illustrated by roentgenograms and clearly diagrammed.

The angiographic diagnosis of intracranial tumors rests upon alterations in the cerebral vascular tree, which may be manifested in the following ways: (1) displacement of the vessels by the direct effect of the tumor, by the more remote effect of edema of a hemisphere, or by ventricular dilatation due to blocking of the cerebrospinal fluid pathways; (2) stretching of vessels by infiltration of brain substance by tumor tissue; (3) presence of hypertrophied or pathological blood vessels; (4) absence of normal vessels; (5) alterations in the order of filling of the vessels and in the circulation time.

The findings in 183 histologically verified tumors and space-occupying lesions are considered in detail. These vary with the type of tumor, its rate of growth, site, blood supply, and vascular pattern. This series included 108 gliomas, 13 metastatic carcinomas, 42 meningiomas, 13 cerebral abscesses, and 7 pituitary and suprasellar tumors. Numerous diagrammatic sketches are given outlining the tumor and the vascular structures, as well as excellent reproductions bringing out various diagnostic points as, for example, the "staining," stellate arrangement of vessels, and coiled vessels adjacent to gliomas.

This article represents a tremendous amount of careful work. It is an excellent review.

Thirty-eight roentgenograms; 98 drawings and diagrams; 3 illustrations in color.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Radiologic Study of Cerebral Angioma.** Guido Lombardi. *Radiol. med. (Milan)* 37: 16-35, January 1951. (In Italian)

This excellent paper follows several others which have recently come out of the Radiological Section of the

Neurological Institute of Milan. The author points out that cerebral angiomas have not been considered very frequent by the older neurosurgeons because up to a few years ago satisfactory diagnosis could not be made. With the advent of angiography, the reported frequency of cerebral angiomas has greatly increased. The clinical indications for cerebral angiography are: (1) convulsions, (2) subarachnoid hemorrhage, (3) hemiplegia, (4) cerebral atrophy as demonstrated by encephalograms or ventriculograms.

The technic used by the author consists in the injection of 10 to 15 c.c. of contrast medium in the internal carotid, with five roentgenograms obtained at intervals of one second. Anteroposterior and lateral views are taken. Contraindications to the examination are high blood pressure and recent hemorrhagic phenomena. The author suggests that in the presence of a recent hemorrhage, the examination be delayed one or two weeks, and that thorotrast be employed instead of iodine preparations.

The radiographic picture of angioma is made up of the afferent vessels, of the capillary stain, and of the efferent vessels. The author points out that the efferent vessels usually have a cylindrical shape because they receive an increased amount of blood from the many capillaries of the angiomatous lesion. The presence of an angioma destroys the balance of the cerebral circulation, inasmuch as the blood which was to feed the brain tissues of the affected side is short-circuited through the angiomatous channels. This explains the brain atrophy which has been frequently found on the side of the angioma and also the presence of collateral circulation through the circle of Willis.

Eleven cases of cerebral angiomata are presented, illustrated by 25 roentgenograms.

CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Shortening of the Posterior Wall of the Sella Turcica Caused by Dilatation of the Third Ventricle or Certain Suprasellar Tumors.** Bernard S. Epstein. *Am. J. Roentgenol.* 65: 49-55, January 1951.

This communication is concerned with shortening of the posterior wall of the sella turcica with or without sellar enlargement or atrophy. In patients without sellar enlargement such shortening appears to be limited to those in whom a suprasellar or parasellar mass impinges upon the posterior clinoids. Good examples of this are seen in the craniopharyngioma group in which several instances of shortening of the posterior wall were observed with a sella of relatively normal size and good bone density. Extrasellar extension of pituitary adenomas may likewise cause such a change. Pneumoencephalograms in these cases showed no dilatation of the ventricular system, since the tumor was not large enough to reach the foramen of Monro. The appearance of the third ventricle in these cases indicated that this structure played no part in the shortening of the wall.

Shortening of the posterior wall of the sella turcica may also occur with certain midline lesions which cause pronounced dilatation of the third ventricle. The floor of the third ventricle in such cases may impinge against the posterior wall of the sella and pro-

trude downward into the cisternae interpeduncularis and pontis.

Seven roentgenograms; 2 photographs.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Intracranial Calcification Probably Due to Toxoplasmosis.** R. Le Bihan, R. Boisot, and C. Lagarde. *J. de radiol. et d'électrol.* 32: 100, 1951. (In French)

A 13-month-old child was seen with a persistent fever, atrophic chorioretinitis, and a bilateral positive Babinski sign, as well as evidence of mental deficiency. Roentgenograms of the skull revealed symmetrical calcification in each lateral ventricle, including both the body and temporal horn. It is stressed that in the presence of intracranial calcifications, atrophic chorioretinitis, and neurologic defects, the diagnosis of toxoplasmosis should be strongly considered. [The agglutination test is a further aid in the diagnosis.—C. M. N.]

Two roentgenograms. CHARLES M. NICE, M.D.  
University of Minnesota

**Pneumoencephalographic Changes Following Prefrontal Leukotomy (Freeman-Watts Technic).** Isadore Meschan and Joe B. Scruggs. *Arch. Neurol. & Psychiat.* 65: 60-71, January 1951.

This is a report of 19 cases in which pneumoencephalographic studies were made before and after prefrontal leukotomy, (see also the authors' paper in *Radiology* 56: 222, February 1951). Here greater emphasis is placed on the autopsy findings, and a brief psychiatric evaluation is included.

Twelve roentgenograms; 2 photographs; 1 table.

**Observations on a Case of Idiopathic Hypoparathyroidism.** Arthur Jordan and A. R. Kelsall. *Arch. Int. Med.* 87: 242-258, February 1951.

A case of idiopathic hypoparathyroidism in a boy of seventeen is presented in considerable detail. Roentgenologically symmetrical intracerebral calcification was demonstrable. It was thought possible that this involved the choroid plexus, though calcification involving the region of the basal ganglia is more usual in such cases. The clinical manifestations responded to correction of hypocalcemia by a high calcium intake, but roentgenograms showed no change in the calcification within the brain.

Four roentgenograms; 4 photographs; 1 chart; 3 tables.

### THE CHEST

**Single, Circumscribed, Intrathoracic Densities.** Hans Abeles and David Ehrlich. *New England J. Med.* 244: 85-88, Jan. 18, 1951.

A follow-up is given on 44 patients in whom single circumscribed lesions were found on survey chest films. A complete study was made in each case in an attempt to make a diagnosis, including history, previous films, additional films, sputum examination, bronchoscopy, and search for a possible primary tumor elsewhere in the body.

Calcification was found to be a reliable indication of a tuberculoma or benign tumor (hamartoma, chondroma, or dermoid). When a lesion could not be called benign (lack of change from older films or presence of calcification) exploratory operation was recommended.

Twenty-one patients were operated upon, and in 8 a malignant lesion was found (5 bronchogenic cancers, 1 thymoma, 1 pleural sarcoma, 1 metastatic). There were 5 uncalcified tuberculomas, and a variety of benign tumors and inflammatory conditions. Operation was advised in 10 other cases but refused (*on advice of the family physicians in 6 of the 10*); 5 of these progressed to the stage of inoperable cancer and 5 remained stable.

All of those in whom operation was not considered necessary remained well a minimum of two years, justifying the conservative management.

It is apparent from this report that a single circumscribed density on a survey film should be regarded as representing a malignant lesion until proved otherwise, and that this fact needs to be brought to the attention of the medical profession generally.

Three roentgenograms. ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**Bronchogenic Carcinoma as a Differential Diagnostic Problem in Pulmonary Disease. I. Carcinoma Arising from Major Bronchi Uncomplicated by Secondary Infection.** John H. Moyer and Alfred J. Ackerman. *Am. Rev. Tuberc.* 63: 176-193, February 1951.

Bronchogenic carcinoma is a common tumor, constituting 6 to 10 per cent of all neoplasms, and the mortality rate is high (5 to 8 per cent five-year survivals) despite advances in surgical treatment. One important cause for the failure of treatment is the late recognition of the disease. There may be few or no symptoms and even when bronchogenic carcinoma is suspected, exhaustive examination fails in some instances to identify or localize it in an early stage. Cough, usually non-productive, is the most common symptom.

There is no unanimity of opinion as to the pathogenesis, and the site of origin has been a subject of controversy. The tumor very likely originates in the undifferentiated cells which line the basement layer of the bronchial mucosa. The cell types are varied; squamous, adeno- and anaplastic types are recognized, the last being found almost exclusively in males. Approximately 75 per cent of the tumors arise from major bronchi, the remainder from the peripheral minor bronchi. The present study deals with lesions of the major bronchi without complicating infection.

A carcinoma arising from a major bronchus is initially limited to the mucosa and, unless obstruction or erosion occurs, no characteristic symptoms or signs are present. There is no parallel between the size of the tumor and the extent of the disease, since widespread metastases are sometimes encountered in patients who have no symptoms or signs referable to the chest or who have small local endobronchial primary tumors. A case is reported in which the primary carcinoma was found at autopsy to be 3 mm. in diameter and situated in the left upper lobe bronchus; nothing had been found to direct the attention of the clinicians to the lung in this patient, who had widespread metastases. This case represents an extreme situation, but it emphasizes the fact that "minimal" lesions without occlusion may not be early lesions.

Partial bronchial occlusion due to a mass projecting into the bronchial lumen or to infiltration of the tumor about the circumference of a bronchus is commonly found in the course of the disease. Clinical and



roentgen findings depend upon the decrease in aeration caused by obstruction and upon ulceration of the mucosal surface of the tumor, which is often present. Blood-streaked sputum is common, with massive hemorrhage occurring only in rare instances. The authors feel that Westermarck's earliest sign of obstruction is transitory and difficult to observe at best. It consists of increased density in the involved segment due to the decreased intra-alveolar pressure which results in hyperemia distal to the blocked bronchus (*Acta radiol.* 19: 285, 1938. *Abst. in Radiology* 32: 750, 1939). During the second stage increased obstruction results in emphysema more pronounced on full expiration than on inspiration, and the third stage is characterized by inspiratory and expiratory emphysema. The fourth stage, atelectasis, follows complete obstruction of the involved segment.

Two cases with localized emphysema are presented to illustrate the non-specific nature of this finding. One patient was found to have an inoperable bronchogenic neoplasm; in the other, no local bronchial disease was found. Careful follow-up to note progression is necessary, as well as repeated bronchography in some cases to detect small alterations in the bronchial tree when no parenchymal masses are present. Bronchostenosis due to lesions other than tumor is often readily differentiated by multiplicity, lack of the irregularity which is noted in tumor, and by separation of stenotic areas by normal bronchus without sharp demarcation. Fifteen roentgenograms.

JOHN H. JUHL, M.D.  
University of Wisconsin

**Angiopneumography and Cancers of the Lung.** P. Santy, M. Bérard, J. Papillon, and J. C. Sournia. *J. franç. méd. et chir. thorac.* 5: 1-9, 1951. (In French)

The authors' technic for angiopneumography entails preliminary sedation with morphine and injection of 60 c.c. of 70 per cent diiodine into the cephalic vein in about one second. Four roentgenograms of the chest are then taken at intervals of one second. In abscess of the lung the vascular pattern is essentially normal. In bronchogenic carcinoma near the hilus there is displacement and/or amputation of vascular shadows. In peripheral pulmonary carcinoma amputation of small vessels is seen.

Fifteen roentgenograms; 8 drawings.

CHARLES M. NICE, M.D.  
University of Minnesota

**On the Significance of Bronchial Perforation in Tuberculosis of the Endothoracic Lymph Nodes, Including Some Remarks about the Publication of Ph. Schwartz.** O. Görgényi-Göttche and D. Kassay. *Schweiz. med. Wehnschr.* 80: 1213-1217, Nov. 11, 1950. (In German)

This is a general discussion on the clinical significance of bronchial perforations of tuberculous lymph nodes, referring to previous publications of the authors and to remarks by Schwartz (*Schweiz. med. Wehnschr.* 79: 454, 1949) who accused them of not understanding the real significance of this process.

Wedge-shaped homogeneous densities in the lung fields of tuberculous children were first described by Kleinschmidt in 1919, and regarded as epituberculous infiltrations. Roessle, a pathologist, found in later years that these are caused by atelectasis. Tubercu-

lous nodes break through and cause a bronchial obstruction.

Radiologically the differential diagnosis between atelectasis and infiltration is often difficult. Planigraphy may be helpful in visualizing the obstruction, as in 22 out of 29 of the authors' cases. Bronchoscopy is particularly important in doubtful cases; of 28 patients, 18 showed a perforation into the bronchus; 3 a narrowing of the lumen due to mechanical pressure from the outside; and in 7 cases the findings were normal. Autopsy studies, however, indicate that only about 53 per cent of all perforations can be diagnosed bronchoscopically.

From their clinical observations, the authors come to the conclusion that the perforation of endothoracic lymph nodes is a pathophysiological process which is, in the majority of cases, of no major clinical importance. It is regarded as a healing process, of daily occurrence in primary tuberculosis. The necrotic material is emptied into the bronchi and is disposed of through the air passages on coughing. The removal of the necrotic material with the bronchoscope can in many cases hasten healing.

Radiologically, one finds a typical wedge-shaped homogeneous density in the affected area. If an obstruction is present, fluoroscopy will reveal a shift of the mediastinal organs toward the side of obstruction on deep inspiration (Holzknecht-Jacobson phenomenon). Four cases are cited in which this phenomenon was observed.

The authors recommend the use of bronchoscopy in such cases, a method which, with our present technic, is without danger in young children and infants.

Two roentgenograms; 1 photograph.

EUGENE F. LUTTERBECK, M.D.  
Chicago, Ill.

**Radiologic Aspects of the Primary [Tuberculous] Infection of the Adult.** G. Voluter. *J. de radiol. et d'électrol.* 32: 75-76, 1951. (In French)

Before 1920, all tuberculous infections in adults were attributed to exacerbation of infantile infection. Then it gradually became known that adolescents and adults may have a true primary infection. There is often a dynamic difference between the primary infection in infants as compared to adults, in that the latter tend more often to present a massive exudative reaction and involve the pleural surfaces. Thus, the primary infection may proceed to give the clinical and radiologic manifestations of tertiary tuberculous lesions.

CHARLES M. NICE, M.D.  
University of Minnesota

**Bronchography in Pulmonary Tuberculosis.** Paul Rabinowitz and Ian S. H. Harper. *Dis. of Chest* 19: 66-77, January 1951.

Bronchography has not been extensively used in tuberculosis, but the authors have found it useful for localization of lesions, for the demonstration of abnormal bronchi and bronchopleural fistulae, and in the differential diagnosis between a contracted and an atelectatic lobe. They present their findings in 109 cases. In 12 the bronchograms were normal, in 83 abnormal, and in 5 unsatisfactory. In 98 of the cases bronchoscopy was also done, and in only 44 did it show evidence of disease: in 16 stenosis of a lobar bronchus, in 21 some localized infiltration, in 6 some



tuberculous infiltration with stenosis, and in 1 extra-bronchial pressure stenosis.

In 51 of the 54 cases with negative bronchoscopic findings, satisfactory bronchograms were obtained; 41 (80 per cent) of these were abnormal; 25 showed "beading," a form of bronchiectasis probably due to present or past tuberculous bronchitis. Stenosis of a lobar bronchus, on the other hand, was diagnosed only 3 times by bronchography as against 16 by bronchoscopy.

The abnormalities demonstrated bronchographically were as follows:

Bronchiectasis	
Beading.....	48
Saccular.....	3
Fusiform.....	12
Cylindrical.....	6
Other Findings	
Cavity.....	4
Bronchopleural fistula.....	2
Stenosis.....	3
Contraction of lobe or segment.....	16
Poor filling of one or more bronchi.....	22
Stump of a bronchus.....	1

The upper lobes were found to be more often the site of bronchographic abnormalities, and in these the posterior and apical segmental bronchi were most often involved. The anterior branch of the upper lobe bronchus was seldom affected. In the lower lobes involvement was predominantly in the apical branches.

The authors used lipiodol for their studies. Residual lipiodol was found in only a few instances and did not prove objectionable. No case of iodism and no spread of the disease was noted.

Two roentgenograms. HENRY K. TAYLOR, M.D.  
New York, N. Y.

#### Changes in Lung Tissues Following Bronchography with Joduron B. W. Vischer. Schweiz. med. Wchnschr. 81: 54-58, Jan. 20, 1951. (In German)

Among the water-soluble media proposed for bronchography in the hope of obviating the occasional undesirable effects of lipiodol is Joduron B, developed by Fischer (Schweiz. med. Wchnschr. 80: 723, 1950. Abst. in Radiology 57: 593, 1951) and consisting of Joduron (50 per cent) in a solution of cellulose glycol acid ether, or carboxymethylcellulose.

Animal experiments have shown that Joduron B disappears from the lungs in three to four hours after injection and is completely absorbed after twenty-four hours. In spite of the early disappearance of the iodine, however, similar changes of the pulmonary tissues were observed as with lipiodol.

Further animal experiments were therefore carried out on 20 rats and 6 guinea pigs, the lung tissues being studied after injection of Joduron B and of cellulose-glycol acid ether alone. The animals were killed and carefully examined at varying intervals, ranging from five hours to four months.

The pulmonary changes were similar in all. After a few hours, the lungs had a reddish appearance due to increase in red blood cells. After twenty-four hours, small yellowish foci were seen, and in some cases the alveoli were obstructed. The carrier material was still present after four months. The cellulose glycol acid ether could be stained with thionin. Characteristic

grayish-white foci which contained many granuloma cells and multinuclear giant cells were seen.

Identical changes were observed in 6 clinical cases in which the lungs were examined from six to ninety days after bronchography. The specimens were obtained after lobectomy.

In view of these observations, the authors have come to the conclusion that bronchography with Joduron B is not without danger. Severe histologic changes are observed, due not only to the iodine but also to the carrier cellulose glycol acid ether, or carboxymethylcellulose, which remains for many months in the lung tissues. These histological changes are identical with severe foreign body reactions, with the formation of multinuclear giant cells. The only advantage in using water-soluble Joduron B lies in the fact that the iodine disappears early and does not interfere with the reading of chest roentgenograms subsequently taken.

Four photomicrographs.

EUGENE F. LUTTERBECK, M.D.  
Chicago, Ill.

#### Nonspecific Pneumonitis of the Left Upper Lobe (Simulating the "Middle Lobe Syndrome" and Producing an Early Superior Pulmonary Sulcus Syndrome). Report of Case. William M. Ashe, John R. McDonald, and O. Theron Clagett. J. Thoracic Surg. 21: 1-6, January 1951.

The authors report a case of a benign lesion of the left lung apex producing changes characteristic of a superior pulmonary sulcus tumor (Pancoast's syndrome). The patient complained of pain anteriorly on the left side of the chest, in the left shoulder, and down the medial side of the arm to the elbow. Roentgenograms demonstrated a left apical consolidation reaching to the first interspace anteriorly and left hilar densities suggesting enlarged lymph nodes. Exploration was done after negative sputum studies for cancer and tuberculosis and negative bronchoscopy. The appearance at surgery also suggested a superior sulcus neoplasm and the upper lobe of the lung was resected. Pathological study demonstrated a non-specific inflammatory condition with marked fibrosis.

This is thought to be the first recorded example of a non-malignant process causing symptoms of the Pancoast syndrome. That the syndrome was not fully developed is thought to be due to the early surgical relief afforded this patient (six weeks). The hilar densities proved to be enlarged peribronchial lymph nodes which were non-obstructing. The authors discuss the "middle lobe syndrome" of non-tuberculous middle-lobe bronchial stenosis, atelectasis, and pneumonitis from enlarged hilar lymph nodes. They believe this case may possibly be an example of a similar syndrome in the upper lobe. Their surgical specimen showed no evidence of extrinsic bronchial compression or bronchiectasis.

Three roentgenograms; 2 photographs; 1 photomicrograph.

DONALD DEF. BAUER, M.D.  
St. Paul, Minn.

#### Subclinical Mineral Oil Pneumonitis. Louis Schneider. New York State J. Med. 51: 245-251, Jan. 15, 1951.

Lipid pneumonitis has been known for more than two decades in marantic children and in chronically ill adults using mineral oil, in whom oropharyngeal

nervous co-ordination is disturbed. Oil aspiration pneumonitis, in persons habitually using oily nose-drop preparations, is well documented. Practically all such preparations have been removed from the market. It is to be noted, however, that in persons with the laxative habit, using mineral oil, similar lung changes can develop. Five or ten years may be required for the pathologic manifestations to appear in otherwise healthy persons, due to the extremely small amounts of oil inhaled with each dose ingested.

The changes are predominantly basal, due to gravity, and may be either diffuse or circumscribed. The diffuse fibrotic alterations, when minimal, are said to be better demonstrated on expiration films. The circumscribed lesions may be mistaken for tumor but are usually surrounded by an interlacing fibrosis. There is no regional adenopathy. The sputum usually shows oil droplets, often for long periods after cessation of intake of the offending agent.

The author cites five case histories which illustrate the salient features of subclinical mineral oil pneumonitis.

Seven roentgenograms; 1 photomicrograph.

JOHN F. RIESSE, M.D.  
The Henry Ford Hospital

**Pulmonary Infiltration with a Positive Wassermann Reaction.** Carlo Borsella. *Ann. radiol. diag.* **23**: 113-124, 1951. (In Italian)

In 1936 Fanconi reported 13 cases of acute pulmonary consolidation in which the Wassermann reaction was positive and stayed positive as long as the consolidation persisted (Schweiz. med. Wchnschr. **66**: 821, 1936). Hegglin and Grumbach (Schweiz. med. Wchnschr. **71**: 578, 1941) reported 19 similar cases in 1941 and suggested that the pulmonary consolidations were probably due to virus pneumonia. Borsella adds another case to those previously recorded and stresses the necessity of repeating the Wassermann test after the radiological and clinical symptoms have disappeared.

Two roentgenograms. CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Kartagener's Triad. Review of the Literature and Report of a Case.** H. S. Zuckerman and L. R. Wurtzbech. *Dis. of Chest* **19**: 92-97, January 1951.

Kartagener's triad consists of a sinusitis, bronchiectasis and situs inversus. The authors report a case in a 63-year-old man, with other associated abnormalities.

Approximately 40 cases have been recorded in the literature. Because of the transposition of the viscera, there is speculation as to a congenital origin of the bronchiectasis. Adams and Churchill (*J. Thoracic Surg.* **7**: 206, 1937) observed 23 cases of situs inversus, in 5 of which (21.7 per cent) bronchiectasis was present, while the incidence of bronchiectasis in approximately 240,000 general hospital admissions was only 0.306 per cent. According to Mallory (*New England J. Med.* **237**: 795, 1947) this high incidence of bronchiectasis in patients with situs inversus may be accepted as indirect evidence in support of its congenital origin.

Seven roentgenograms.

HENRY K. TAYLOR, M.D.  
New York, N. Y.

**Coccidiomycosis: A Review.** *Progress of Medical Science.* J. Schwarz and J. Muth. *Am. J. M. Sc.* **221**: 89-107, January 1951.

A review of the literature on coccidioidomycosis, with a section on the roentgen findings. A bibliography of approximately 290 references.

**Posterior Mediastinal Goitre: A Report of Three Cases.** J. S. Tomkinson. *Brit. J. Surg.* **38**: 271-275, January 1951.

Three cases of goiter in the posterior mediastinum are reported. The author believes that the x-ray appearances are characteristic and must be appreciated if a correct diagnosis is to be made. In the antero-posterior film the thoracic extension of the goiter is seen, but there is nothing significant to indicate the posterior position. This is shown in the lateral film, for the tumor lies behind the trachea, usually pushing it forward, and there is no swelling in front of the trachea compressing it. In 2 of the 3 cases recorded here, it was known that the tumor arose from the thyroid, but the posterior position was not recognized despite the x-ray appearances. In the other case the posterior position was recognized but the nature of the swelling was mistaken.

The anterior displacement and curvature of the trachea are clearly demonstrated in the illustrations.

Seven roentgenograms; 2 photographs.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Posterior Pneumomediastinum.** L. Condorelli, A. Turchetti, and G. Pidone. *Ann. radiol. diag.* **23**: 33-54, 1951. (In Italian)

The authors describe a technic for the production of gaseous contrast in the posterior mediastinal space, consisting in injection of 200-300 c.c. of oxygen by means of a needle inserted through the trachea in the midline just above the jugular notch. The needle perforates both walls of the trachea and its point should rest between the posterior wall of the trachea and the anterior wall of the esophagus. The radiographic studies include anteroposterior and lateral films and anteroposterior and lateral laminagraphs.

The appearances obtained by this technic in normal subjects are described, and several excellent illustrations are presented in which the posterior mediastinal structures are clearly dissociated. The authors promise to follow this article with one on the pathological lesions discovered by this method. In the opinion of the abstractor, this work is of great interest and the technic should be of help in clarifying difficult cases of mediastinal disease.

Twenty-three roentgenograms; 2 drawings.

CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Endothelioma (Mesothelioma) of the Pleura. A Review with a Report of Seven Cases, Four of Which Were Extirpated Surgically.** Lew A. Hochberg. *Am. Rev. Tuberc.* **63**: 150-175, February 1951.

Pleural mesothelioma or endothelioma is a rare tumor, having occurred in only 0.07 per cent of 60,042 autopsies collected by the author from various sources. There is some controversy as to the proper term to use in describing this tumor. While it is primary in the pleura, the exact origin of the cells is a matter of

dispute among various investigators. "Endothelioma" is the most commonly used designation, but "mesothelioma" is somewhat more inclusive. It is generally agreed that the serosal tissue (pleura) is derived from mesoderm and that tissues derived from the mesoderm may have prominent glandular function, as well as functions related to blood and lymph vessel formation. Therefore, the cells are multipotential embryologically and may give rise to a rather wide variety of tumor cells. The exact cell of origin is not definite.

Endothelioma may arise from the visceral or parietal pleura, and two gross types are recognized: (1) a circumscribed tumor which appears to spring from the surface of the pleura and (2) a diffuse growth of variable thickness which presents an uncertain focus of origin. The latter is the more common and is the more extensive. It consists of solid cords or hollow tubes of cells which sometimes seem to secrete a mucinous material. These cells are distinctly of an epithelial appearance and sometimes suggest the hyperplastic proliferation of vascular endothelium but more often seem truly epithelial, with cuboidal or cylindrical cells arranged about lumina. The circumscribed or localized tumors resemble fibroma or fibrosarcoma and do not have epithelial elements. Often there is extensive fibrosis of the pleura associated with the tumor, tending to give it a scirrhous appearance. Within the same tumor the cells may manifest notable pleomorphism.

The greatest number of reported cases occur between the ages of forty and sixty years, with extremes of five to over seventy. The ratio of males to females is 1.8 to 1.0. Symptoms are minimal or absent at the onset; localized pain and slight respiratory difficulty appear relatively early and progress to severe pain and marked dyspnea. Cough is often present, and in the late stages there are marked cachexia, dyspnea, cyanosis, and pain. Low-grade fever may be present. The physical findings are those of pleural tumefaction, often accompanied by local tenderness. Pleural fluid is commonly present in varying amounts. The fluid may be serous or serosanguineous, but is usually quite hemorrhagic, and aspiration affords little relief of dyspnea. Although tumor cells can be found in the fluid, cytodiagnosis is often difficult if not impossible. On failure to establish the diagnosis by cytologic study, exploratory thoracotomy is indicated. Therapy is usually confined to palliative irradiation, although it is possible that surgical extirpation might be successful in early cases.

Roentgenographic findings depend upon the type of tumor; it may be well circumscribed and have a sharp or irregular border. Pleural fluid may obscure the lesion. In the later stages, roentgenograms obtained following removal of the fluid will fail to show much reduction in the opacity of the involved hemithorax due to the increasing thickness of the tumor. Tumor nodules are often present in addition to the diffuse thickening of the pleura. These findings are not characteristic, but should lead to the suspicion of primary pleural tumor in the absence of other obvious cause. Rapid re-accumulation of fluid is also of some significance. One of the most useful procedures in the roentgenographic diagnosis of endothelioma of the pleura is the induction of a pneumothorax after removal of the fluid. Roentgenograms should be taken immediately after the air is introduced. Overexposed plates taken at this time will usually show tumor

nodules on the surface of the pleura.

Seven cases are presented, illustrative of the histologic types. In 3 of the cases the tumor was relatively circumscribed, while in the other 4 it was diffuse and associated with varying amounts of pleural fluid.

Thirteen roentgenograms; 16 photographs; 14 photomicrographs.

JOHN H. JUHL, M.D.  
University of Wisconsin

**Solitary (Localized) Mesothelioma of the Pleura.**  
Arthur Purdy Stout and George M. Himadi. *Ann. Surg.* 133: 50-64, January 1951.

The authors state that the most common of the rare primary tumors of the pleura is a solitary circumscribed fibrous growth which either projects into the pleural cavity or else extends from the pleura into the lung or chest wall. When projecting, these tumors are differentiated and benign; when buried, they are anaplastic and malignant. Some of the names that have been used previously to describe them are fibroma, fibrosarcoma, fibrosarcoma myxomatodes, myxosarcoma, leiomyosarcoma, sarcoma, sarcoma-like tumor, giant sarcoma of the pleura, endothelioma, and endothelial sarcoma. The tumors are composed of spindle-shaped cells and connective-tissue fibers in a unique arrangement. Since in one of the authors' cases the cells when explanted *in vitro* grew in a fashion characteristic of mesothelial cells, they believe the tumors should be called mesotheliomas and distinguished from diffuse mesotheliomas by the adjectives solitary or localized.

In each of the 8 cases presented, roentgen examination disclosed evidence of a solitary intrathoracic mass. From the point of view of the roentgenologist, these tumors may be divided into three groups:

1. Solitary tumors in contact with the chest wall, which project into the pleural cavity.
2. Tumors lying within an interlobar fissure.
3. Tumors which appear to be within the lung parenchyma but actually are attached to the visceral pleura and either project outward from the pleural surface or are embedded within the lung. The tumors have no distinctive roentgen characteristics which would differentiate them from numerous other solitary tumors of the chest but should be considered in the differential diagnosis.

Since these tumors grow slowly and metastasize sparingly, surgical excision is favorable and is the treatment of choice.

Ten roentgenograms; 5 photographs of gross specimens; 9 photomicrographs.

WILLIAM H. SMITH, M.D.  
University of Louisville

**Interlobar Pleurisy in a Cardiac Patient.** J. Reboul and P. L. Martin. *J. de radiol. et d'électrol.* 32: 112-113, 1951. (In French)

A 69-year-old man presented a picture of cardiac failure with effort and nocturnal paroxysmal dyspnea, oliguria, ankle edema, etc. No pulmonary symptoms such as fever, cough, or expectoration were noted. In the chest roentgenogram there was a soft rounded opacity, about 8 cm. in diameter, in the lateral right mid-lung field. The border was sharp in outline. In the lateral view the opacity was ovoid from before

backward and seemed to extend along the fissural pathway. A second homogeneous density with shading border appeared in the right paracardiac region. Clinical and radiologic amelioration followed cardiac therapy. Part of the paracardiac shadow persisted, however, and a linear shadow remained in the horizontal fissure. The patient died of cardiac insufficiency eight months later and evidence of pleural involvement in the above-mentioned areas was confirmed postmortem. Although unusual, interlobar effusion should be remembered as a possibility in cardiac patients presenting rounded opacities in the chest roentgenogram.

Four roentgenograms. CHARLES M. NICE, M.D.  
University of Minnesota

**Anatomy of the Heart and Great Vessels: Angiocardiographic Study.** J. E. Miller. Texas State J. Med. 47: 5-9, January 1951.

The conventional points concerning angiocardiography are made, but the author is most emphatic about one point, which is well taken and is too often neglected in the departments of anatomy of the medical schools—that the most accurate method of studying cardiac anatomy is in the living person, with angiocardiography. This point is emphasized by comments concerning the changes in position and relationships which take place following the removal of the pressures from the circulatory system.

Twelve roentgenograms. S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Measurement of Heart Size.** Geoffrey Bourne and B. G. Wells. Lancet 1: 17-18, Jan. 6, 1951.

The authors describe a simple method of measuring the heart size, using a standard x-ray screening set of the type in which the tube and shutters may be moved horizontally or vertically while the screen remains stationary. This is in contrast to the more usual arrangement in which the tube and screen are coupled so that the tube may not be moved without moving the screen with it. The patient is placed standing behind the screen and facing the examiner, and his position is adjusted, by palpation of the shoulders, chest, and hips, so as to ensure that the transverse plane of the chest is parallel with the screen. He is told to lean firmly forward and to press the shoulders and upper part of the chest as near to the screen as possible, the arms hanging to the sides. He is also told to stand with the feet firmly apart to prevent swaying.

When a general view of the chest has been obtained, the vertical shutters are closed until the field is rather less than an inch wide. The tube and shutters are moved until the right border of the heart lies in the center of this narrow vertical field. The position of this border is marked on the screen by a vertical grease-pencil line. The tube and shutters are then moved until the left border of the heart is in the center of the field, and this border is marked in a similar manner. Measurement is taken after a full easy inspiration, at the end of which the breath is not held in. The patient is asked to "breathe deeply into the stomach," and by observing the diaphragm it can be confirmed that the depth and character of the inspiration are natural and full. The heart is measured in diastole. Systole does not seem to influence the position of the right border to any appreciable extent,

but on the left side there may be in some cases nearly a centimeter difference between the two cardiac phases.

To test the degree of accuracy of the method, 53 persons were investigated, three separate "blind" measurements being made in each case. In 77 per cent of the 159 measurements of heart size the divergence between the three separate measurements was 0.5 cm. or less, and in 92 per cent it was 0.6 cm. or less.

One illustration.

**Diagnosis of Heart Disease. Conventional Roentgen Examination.** A. G. Barsh. Texas State J. Med. 47: 9-14, January 1951.

The author believes that most cardiac lesions can be suspected, if not accurately diagnosed, by conventional methods of radiologic examination in correlation with the clinical findings. Variations in the bony thorax and the pleuropulmonary structures are significant in the differential diagnosis.

The various diseases and congenital anomalies involving the heart are reviewed and the characteristic findings are discussed. It is pointed out that of the congenital anomalies that are amenable to surgery 80 per cent can be recognized by an astute clinician with the aid of conventional roentgen study.

Of the cyanotic infants who survive beyond two years, about 70 per cent have tetralogy of Fallot. In this condition the hilar markings are thin, the pulmonary segment of the left border of the heart is depressed, and the lower left pole of the heart is prominent in the frontal projection as a result of right ventricular enlargement. Persistent right aortic arch is present in about one-fifth of the cases. Since the primary indication for the Blalock anastomosis is the presence of a tetralogy of Fallot, any gross variations in the roentgen picture such as marked cardiac enlargement or large pulmonary vessels are indications for the more specialized diagnostic procedures.

Eisenmenger's complex consists of the same basic defects as tetralogy of Fallot but there is no pulmonary stenosis. The cardiac enlargement is more marked, the pulmonary artery is prominent, and the lung fields show a normal or prominent vascular structure.

Patent ductus arteriosus is not diagnosed by the roentgen findings, but this examination can be suggestive or confirmatory.

Coarctation of the aorta can be identified roentgenologically by the small aortic arch, dilated ascending aorta, prominent subclavian artery, and irregular notching of the inferior borders of the ribs. The heart may be normal in size, but it frequently shows mild enlargement of the left ventricle.

With small interauricular defects, there may be no significant roentgen changes. If the defect is large, the heart is tremendously enlarged and globular in shape. The pulmonary artery is prominent, and the aortic arch is frequently not visualized. With inter-ventricular defects there may be little change in heart size; the aortic arch is prominent, as is the pulmonary artery.

Twenty-one roentgenograms.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Auricular Septal Defects in Children.** John D. Keith and Constance C. Forsyth. J. Pediat. 38: 172-183, February 1951.

Auricular septal defect was found to be the sixth



commonest congenital abnormality of the heart encountered in the cardiac outpatient clinic of the Hospital for Sick Children, Toronto. A summary is presented of 14 cases with evidence of an atrial septal defect confirmed by cardiac catheterization.

The average age of the patients was 7.7 years. There were 11 females and 3 males in the group. Three-quarters of the patients were thin, but the remainder were of average physique. The exercise tolerance was good in 5, moderate in 7, and poor in 2. All of the children were acyanotic with the exception of one with transient heart failure, who showed a minor degree of cyanosis of the lips which disappeared as the failure was relieved. Nearly every child had some increase in the force of the heart beat which was readily determined by palpation. In a single instance there was a palpable thrill. All of the group had systolic murmurs up the left border of the sternum. This was maximum at the level of the first and second interspaces in two-thirds of the patients and maximum at the level of the second and third left interspaces in the others.

All but one of the patients showed enlargement of the heart. Roentgenologically the pulmonary trunk was found to be enlarged in every case. Eleven of the 14 cases in the series showed increased pulsation of the hilar shadows.

Right axis deviation was present in the electrocardiogram in 9 cases. There was no axis deviation in 3 cases and left axis deviation in 2.

Cardiac catheterization was useful in establishing the diagnosis. In 5 instances it was possible to pass the catheter through the defect into the left auricle and on into the pulmonary vein. Oxygen determinations revealed a higher oxygen content of the blood in the right auricle than in the superior vena cava in all cases.

Details of a case treated by surgical closure of the defect are presented. It is concluded that the optimum surgical correction of an auricular septal defect should eliminate the shunt between the auricles and return the heart size and exercise tolerance to normal. This will be difficult to achieve by present technics, but enough has been done to suggest that the problem is not insuperable.

Four roentgenograms; 1 table.

HOWARD L. STEINBACH, M.D.  
University of California

**The Eisenmenger Complex and Its Relation to the Uncomplicated Defect of the Ventricular Septum. Review of Thirty-Five Autopsied Cases of Eisenmenger's Complex, Including Two New Cases.** Arthur Selzer and Gert L. Laqueur. *Arch. Int. Med.* 87: 218-241, February 1951.

Two new cases of the Eisenmenger complex in adults are reported in detail. In addition, data on 33 autopsied cases of this syndrome are tabulated and their clinical and pathological features are reviewed. Following the lead of Saphir and Lev (*Am. Heart J.* 21: 31, 1941) the concept of the Eisenmenger complex is widened to include cases in which the aorta is completely dextroposed, arising from the right ventricle.

Clinical features of the Eisenmenger complex include cyanosis, which is frequently present from birth; non-characteristic systolic and diastolic murmurs with a loud pulmonary second sound; roentgen evidence of striking dilatation of the pulmonary artery and its

branches, associated with pulmonary congestion and increased arterial pulsations; evidence of right ventricular enlargement and hypertrophy in the roentgenogram and electrocardiogram.

Pathological features are a localized high defect of the ventricular septum, usually oval or crescentic, measuring between 1 and 2.5 cm. in longest diameter; varying degrees of dextroposition of the aorta, from minimal overriding to a complete origin of the aorta from the right ventricle; dilatation of the pulmonary artery and its branches, and severe hypertrophy of the right ventricle, with or without some left ventricular hypertrophy.

Microscopic examination of the pulmonary arterioles in the authors' 2 cases revealed severe intimal and medial changes. Such changes have also been noted by others, and it is believed that they constitute a characteristic feature of the Eisenmenger complex, being evidence of long-standing severe pulmonary hypertension.

Further evidence is presented to support the view that no dividing line exists between the uncomplicated defect of the ventricular septum and the Eisenmenger complex, and that both are caused by varying degrees of the same process of maldevelopment.

The pathogenesis of the cyanosis associated with the Eisenmenger complex is considered, and the hemodynamics of the condition are discussed.

Finally, the complex is redefined by a combined pathological and physiological set of criteria, namely (a) a high, localized defect of the ventricular septum, (b) a position of the aortic orifice in relation to the defect which permits an admixture of venous blood to enter the aorta, as evidenced by anoxemia, and (c) an absence of significantly elevated resistance at the pulmonary outflow tract of the right ventricle.

Nine illustrations, including 2 roentgenograms; 3 tables.

**Disorders of the Cardiovascular System Occurring with Catheterization of the Right Side of the Heart.** Walter T. Zimdahl. *Am. Heart J.* 41: 204-216, February 1951.

After a review of the literature on temporary complications associated with catheterization of the right side of the heart, the author presents 2 cases. In 1 patient a nodal tachycardia developed with the catheter in place. The arrhythmia did not cease spontaneously after thirty minutes and was terminated by treatment. In the second patient, with a tetralogy of Fallot, a complete auriculoventricular heart block developed one day after the catheter had been removed. Second-degree heart block then appeared, followed by first-degree auriculoventricular heart block; the electrocardiogram returned to normal in seven days.

Complications reported by others are tabulated, and the importance of a trained team and meticulous technic in the performance of heart catheterization is stressed.

Three electrocardiograms; 1 table.

**Transient Right Bundle Branch Block Produced by Heart Catheterization in Man.** Ernst Simonson. *Am. Heart J.* 41: 217-224, February 1951.

In a 50-year-old man with pulmonary hypertension and right ventricular strain pattern, heart catheterization produced transient complete right bundle branch



block which persisted for one hour and was followed by gradual recovery during the next twenty minutes. Some electrocardiographic changes persisted for several days. Instances of transient right bundle branch block produced by heart catheterization, reported by others, are mentioned. Even more serious lesions, such as ventricular fibrillation, have occasionally been observed. These cases emphasize the necessity of caution and careful selection of patients for heart catheterization.

Five figures.

**Superior Vena Caval System Obstruction.** Malcolm C. McCord, Philip Edlin, and Malcolm Block. *Dis. of Chest* 19: 19-27, January 1951.

This report is based upon 11 cases of superior vena caval obstruction, 3 due to aortic aneurysms; 3 to bronchogenic carcinomas; 1 to superior mediastinal lymphoma, 1 to post-mediastinitis scarring; 1 to acute mediastinal herniation of cystic lung; 1 to thrombosis of the right innominate vein occurring during an episode of cardiac decompensation; and 1, with occlusion of both innominate veins, to a syphilitic innominate artery aneurysm. Obstruction was caused by extrinsic pressure, by invasion of the vein wall by neoplasm, or by thrombosis. The symptoms were attributable to or overshadowed by the underlying disease processes. In those cases with long-standing obstruction, no symptoms were present, since adequate collateral circulation had developed. Two cases presented an acute picture; in the other 9 the course was chronic. All showed evidence of venous distention in the neck, upper portion of the body, or arms; in 3, collateral channels were visible.

Chest phlebograms were obtained in 7 cases, showing the anatomical site, degree of obstruction, presence and distribution of collateral channels, and retardation of flow in the obstructed vessels.

Four case histories with roentgenograms are included.

HENRY K. TAYLOR, M.D.  
New York, N. Y.

**Thrombosis of the Terminal Aortic Bifurcation. Clinical and Aortographic Study.** G. Bonte and J. Desruelles. *J. de radiol. et d'électrol.* 32: 15-20, 1951. (In French)

At times, patients with thrombosis of the distal aortic bifurcation present less severe symptoms (claudication, etc.) than those with thrombosis of popliteal or leg arteries. This has been attributed to collateral circulation. However, some patients do have typical intermittent claudication. Leriche has called attention, also, to such symptoms as lack of penile erection and apparently banal symptoms usually attributed to neuritis, sciatica, or rheumatism. Absence of femoral pulse is a strong presumptive sign, but collaterals may result in a weak femoral pulse. Diminution of the Achilles reflex is not uncommon. A good number of patients are of Slavic origin (Russian, Polish, Ukrainian). After a long period of tolerable ischemia, there may be rapid development of gangrene. Embolic phenomena may play a part in cases of mitral heart disease and bacterial endocarditis.

For aortography, the puncture is made at the level of the third or fourth lumbar vertebra, below the origin of the major branches of the abdominal aorta. Since there is danger of too much pressure on injection,

which is harmful to small vessels, manual pressure on the syringe is preferable to the use of mechanical devices. After injection of 20 c.c. of contrast medium, an immediate film is taken. This shows the abdominal aorta and principal branches. In thrombosis of the aortic bifurcation, a film taken two to five seconds later will demonstrate collaterals.

Two cases are presented in patients with bacterial endocarditis. In one, death ensued rapidly. In the other, massive doses of penicillin apparently aided recovery.

Seven roentgenograms; 1 photograph.

CHARLES M. NICE, M.D.  
University of Minnesota

## THE BREAST

**Diagnosis of Tumors of the Breast by Simple Roentgenography. Calcifications in Carcinomas.** Raúl Leborgne. *Am. J. Roentgenol.* 65: 1-11, January 1951.

The author believes that roentgen study of the breast should now be included in the clinical investigation of mammary disease. This, however, because of the slight difference of opacity between normal and pathologic tissues, demands a perfect technic.

In the Institute of Radiology and Cancer Center of the Ministry of Public Health, at Montevideo, Uruguay, from which this report comes, a craniocaudal projection is employed. First, a topographic roentgenogram is made, with a cone large enough to cover the total area of the breast. Then a second film is exposed, localizing the exact site of the tumor, with the smallest possible cone, so as to reduce secondary radiation. Since tumors near the upper portion of the breast are not seen clearly in the craniocaudal projection, this technic must be complemented by a lateral film study. The factors are: focus-film distance 60 cm., 30 kv. (peak), 5 ma.-sec. for each centimeter thickness of breast. Non-screen films are employed.

Encapsulated benign tumors, fibroadenomas, and cysts produce rounded or multilobulated images with smooth borders, sometimes partially or wholly surrounded by a transparent halo separating them from the adjacent mammary tissue.

The usual roentgen shadow of adenocarcinoma varies from 1.0 to 4.0 cm. in diameter. The borders are ragged, with numerous spicules of variable lengths radiating from the periphery into the surrounding tissue. This "spiculated" border is characteristic of malignant growth and indicates an eminently scirrhous nature. Occasionally a malignant tumor may present a smooth border, in which event a differential diagnosis may be difficult. The shadow of the tumor is uniformly dense, sometimes containing a scattering of multiple punctate calcifications resembling fine grains of salt, generally clustered in a region of the breast. These calcifications, which at first might pass as defects in the film, may be found (1) inside the tumor nodule, (2) inside and surrounding the nodule, (3) as the only roentgen sign, that is, without any nodular image.

The author stresses the importance of these calcifications. He believes that their recognition and demonstration constitute one of the easily observed aspects in which mammary cancer is presented.

Thirty-five illustrations, including 27 roentgenograms.

DANIEL WILNER, M.D.  
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### THE DIGESTIVE SYSTEM

**Behavior of Carob Gum in the Gastrointestinal Tract of Man.** Arthur Andrews Holbrook. *Am. J. Digest. Dis.* 18: 24-28, January 1951.

Studies were carried out comparing a laxative called "Vacuosa," the active principle of which is the hemi-cellulose of the carob seed, with psyllium seed gum and karaya gum. All these vegetable gums have hydrophilic properties.

Peloids were made of each of the three laxatives mixed with barium, and these were given to three groups of people. The first group had no bowel complaints, the second group complained of constipation, and the third had diarrhea. Serial films were obtained at various intervals and were studied with reference to disintegration of the peloids, rapidity of progress of the substance through the bowel, increase in the bowel content, etc. It was found that the Vacuosa peloids retained their identity for the first three hours after their ingestion, so that in most cases they were in the large bowel before they disintegrated, while the psyllium seed pellets and the karaya pellets disintegrated a short time after ingestion. With the two latter preparations, there was a sense of fullness of the abdomen that was not present in patients taking Vacuosa. This is probably to be attributed to the early disintegration of the peloids with resultant swelling.

There was not much difference in the action of the three gums. None of the patients showed any harmful effects.

The conclusion drawn from the studies is that Vacuosa is a safe laxative that disintegrates at the optimum time in the intestinal tract. It forms a colloidal gel which clinically affects stools in a way which makes them "easier to pass" and assists in promoting normal stool habits by causing an increase in bulk which is soft, homogeneous and non-irritating.

Twenty-four roentgenograms; 1 graph.

JOSEPH T. DANZER, M.D.  
Oil City, Penna.

#### Effects of Hexamethonium Bromide on the Stomach.

A. H. Douthwaite and M. G. Thorne. *Brit. M. J.* 1: 111-114, Jan. 20, 1951.

The effects of hexamethonium bromide (C6) on gastric secretion and motility were studied by subjecting a group of 10 patients to a series of radiological studies and test meals. Nine of the group had radiological evidence of duodenal ulcer; one had no evidence of it. All had been subjected to test meals before. This is considered important by the author because it decreased the emotional factor.

The gastric motility and emptying time were measured by giving a barium meal following a fasting period of twelve hours. The progress of the meal was observed fluoroscopically until it entered the duodenum and examinations were done half an hour later and at hourly intervals thereafter. The points particularly noticed were the tone of the stomach, the amount of peristalsis, and the emptying time. All of these patients had highly motile stomachs. Barium passed into the duodenum either immediately or within four minutes after its ingestion. After half an hour 9 of the 10 stomachs had emptied themselves of about four-fifths or more of their contents, the tenth being half emptied, and the barium was distributed throughout

the jejunum, having traversed the duodenum, leaving it nearly void of radiopaque material.

Three days after the control test, 7 subjects were given 100 mg. of C6 intramuscularly, and a half hour later received a barium meal. The half-hour films differed markedly from the controls. In no case was the stomach more than one-fourth empty. Most of the barium was seen in the duodenum and first portion of the jejunum, which appeared as immobile dilated segments of bowel so loaded with barium that the mucosal pattern was obliterated. This dilatation continued up to six hours after administration of the drug. Some of the subjects were given C6 every four hours for seven days and their gastric motility was again studied. Four of the subjects showed less dilatation and greater motility than after the single dose; the rest appeared to react in about the same manner.

Seven patients with duodenal ulcer were also given gruel test meals after intramuscular injection of C6. Their acid curves were not markedly altered, except in one case, in which achlorhydria followed.

The side effects of the drug appeared to be fairly severe; of the 10 subjects, 6 fainted on standing. Tachycardia, dryness of the mouth, and visual disturbances were other complaints.

The authors conclude that while this drug is not to be used in ambulatory patients, it may be of benefit in bed patients, particularly at night, because of its prolonged effect.

Six roentgenograms; 2 graphs.

JOSEPH T. DANZER, M.D.  
Oil City, Penna.

**Prolapsing Hypertrophied Gastric Mucosa Simulating a Prolapsing Gastric Polyp. Report of Case.** Maurice Feldman and Zachariah Morgan. *Gastroenterology* 17: 83-87, January 1951.

The authors report what they believe to be a rare case of prolapsing hypertrophied gastric mucosa simulating a prolapsing gastric polyp. They stress the evasive qualities of these two conditions during roentgen examination.

Three roentgenograms. C. R. PERRYMAN, M.D.  
Pittsburgh, Penna.

#### Pyloric Obstruction Due to Sarcoid of the Stomach.

Adolph A. Appell, Harold G. Pritzker, and Philip G. Klotz. *Arch Surg.* 62: 140-144, January 1951.

A case of solitary sarcoid of the stomach is presented, apparently the third such case on record. The symptoms were those of pyloric obstruction. The roentgenogram revealed a pyloric obstructing lesion of undiagnosed type, with 80 per cent gastric retention after six hours. A subtotal gastric resection was performed and the diagnosis was made histologically. No lesions were found in other viscera.

One roentgenogram; 2 photomicrographs.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Observations of Normal and Abnormal Human Intestinal Motor Function.** E. Leonard Posey, Jr., and J. Arnold Bargen. *Am. J. M. Sc.* 221: 10-20, January 1951.

This is a report of a study of intestinal movements in 24 patients with ileac and/or colonic stomas. The technic used was that described by Posey *et al.* (*Proc.*

Staff. Meet., Mayo Clin. 23: 297, 1948), employing two balloons mounted in tandem, an optical manometer, and a photokymograph.

From this study it is apparent that intestinal motor function is a complex form of activity made up of three basic components: tone, motility of various types, and the intersegmental relationships, including co-ordination and incoordination. Tone provides the general background upon which motility is superimposed. It is possible for excessive tone markedly to inhibit motility.

The intestinal tract is composed of functional segments, smaller in the ileum than the colon, which usually behave independently of one another. This normal intersegmental incoordination is of prime importance in acting as a physiologic "brake" to prevent the too rapid aboral progression of intestinal contents. The intestine cannot transport its contents unless adjacent functional segments become coordinated to act together, in phase, as single motor units. Excessive intersegmental coordination has been recorded from both the colon and the ileum of patients with chronic ulcerative colitis. Excessive intersegmental incoordination produces cramping and discomfort.

It was not possible to confirm the "law of the intestine" (relaxation of distal segment concomitant with propulsive peristalsis in the proximal segment) completely; ascending and descending excitations from a point of stimulation were constantly observed in 6 patients. The gastrocolic reflex was not conclusively demonstrated in 3 patients. No alteration of motility patterns was observed during sleep. Conduction of motility was not found to cross the transected bowel. A dissociation of activity between the small and large intestine was noted in 1 patient. Unused segments of the bowel are potentially capable of normal motility.

Five figures; 1 table.

#### Intestinal Obstruction in Infants and Children.

Kenneth C. Sawyer and Horace P. Marvin. Arch. Surg. 62: 1-13, January 1951.

The treatment of intestinal obstruction in childhood is primarily operative and of an emergency nature. Prompt diagnosis is therefore essential. Pain—colicky in nature, with relief between spasms—is the earliest and most constant symptom, usually accompanied with abdominal distention. With strangulation, there is constant pain between the attacks of colic. Vomiting is progressive in frequency and amount. When obstruction is high, the vomitus contains only milk or food. With obstruction below the papilla the vomitus may contain bile. With low obstruction, it becomes foul-smelling, sometimes with a fecal odor.

Roentgenography plays an important role in diagnosis, but the authors are doubtful about the advisability of administering barium by mouth. Much can be learned from the judicious use of anterior, posterior, and lateral roentgenograms. Distended loops of bowel are significant in the absence of gas in the colon. The distended intestinal coils are arranged in a transverse position, and the valvulae conniventes remain distinct, since the bowel may contain a little liquid, but mostly gas. As the blockage progresses, the pattern becomes more pronounced, until a "stair-step" arrangement of the proximal distended bowel develops. In contrast, there is no characteristic

pattern when strangulation is present, and the valvulae conniventes are indistinct or not seen. This condition is due to the extravasation of blood or serum into the strangulated loops.

The authors discuss the various etiologic types of intestinal obstruction and report illustrative cases:

(1) *External Hernia*: It is believed that strangulated external hernia is a cause of intestinal obstruction in children more often than has generally been believed. As a rule, the diagnosis is obvious.

(2) *Bands and Adhesions*: These are uncommon in children because of the low incidence of surgical procedures.

(3) *Volvulus*: This is due to defective fixation of the mesentery. In order for a volvulus to occur, there must be an axis having one or more fixed points, about which the bowel rotates. The axis is usually a congenital or acquired anomaly, such as a band between a Meckel's diverticulum and the umbilicus, or an adhesion secondary to intraperitoneal inflammation.

(4) *Meckel's Diverticulum*: A Meckel's diverticulum can cause obstruction (a) by virtue of a band running from the diverticulum to the inner side of the umbilicus, (b) by acting as a leading point of an intussusception, or (c) by twisting and becoming adherent to the mesentery.

(5) *Intussusception*: According to Wangenstein, about 75 per cent of the patients with obstruction due to this cause are under two years of age. The majority are between the fourth and seventh month of life, and two-thirds of them are males. The cardinal symptoms are intermittent abdominal pain, vomiting, passage of mucus and blood in the stools, and palpable abdominal tumor.

(6) *Malrotation*: This is not rare, although cases in which it is of sufficient degree to produce obstruction of the bowel are infrequent.

(7) *Congenital Atresia*: While congenital atresia is an uncommon cause of obstruction, any child with persistent vomiting during the first two days of life should be examined with this in mind.

(8) *Stenosis of the Rectosigmoid and Imperforate Anus*: An opaque catheter should be placed in the rectal pouch, and the infant examined in an inverted position. The distance between the catheter and the gas shadow indicates the depth of the imperforate anus.

Six roentgenograms; 2 photographs.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

#### Mesenteric Liposarcoma: A Rare Cause of Intestinal Obstruction. John M. S. Manson. Brit. J. Surg. 38: 394-396, January 1951.

A case is reported of liposarcoma arising in the mesentery and producing bowel obstruction. Roentgen examination showed dilatation of the small bowel with numerous fluid levels. At operation, the distal ileum was found bound down to the right lateral pelvic wall by dense adhesions; there was almost complete atresia of the bowel lumen, and large, firm grape-like swellings were present on the adjacent mesentery. One of these latter was removed and proved to be liposarcoma. Six weeks later at a second operation, the remaining masses were found to have enlarged, and other small masses had appeared, but there were no secondary lesions elsewhere in the abdomen. The affected loop of ileum was resected, and an ileo-ileostomy was performed.

The author quotes Stout's classification of liposarcomas (Ann. Surg. 119: 86, 1944) and places this case in the first group: well differentiated myxoid type, which may become enormous but does not metastasize.

Six illustrations, including 2 roentgenograms.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Duodenal Loop Triad Syndrome.** William Snow and Jerome A. Marks. New York State J. Med. 51: 252-254, Jan. 15, 1951.

The duodenal loop triad syndrome, as conceived by the authors, consists of duodenal loop disease, biliary tract disease, and pancreatic involvement. An attempt is made to furnish a pathological-physiological basis for this symptom complex, which is dependent on a variety of courses.

It is reasoned that, since both the biliary tree and the pancreatic tract empty into the second portion of the duodenum, often by a common opening, inflammation of the duodenum, by obstructive reaction, brings about changes in the other two systems. It is felt that many irritative factors, affecting primarily the duodenal loop, can thereby precipitate symptoms attributable to all three systems, and explain some of the more bizarre but vague disturbances of the upper gastro-enteric tract.

The roentgen changes of pancreatic and biliary disease, consisting mainly of abnormal calcification and, in the case of the gallbladder, also functional alterations, are well known. The manifestations in the duodenal loop of dilatation, spasm, and thickening of the plicae circulares may not be generally accorded the specificity with which the authors endow them.

The authors stress that their discussion of this presumptive pathological complex does not purport to explain all the mechanisms of biliary and pancreatic disease. They merely wish to offer a logical approach to diagnosis and treatment of certain important gastrointestinal complaints.

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**Hirschsprung's Disease.** Martin Bodian, C. O. Carter, and B. C. H. Ward. Lancet 1: 302-309, Feb. 10, 1951.

A genetic study was made of the families of 37 children (from a series of 40) with histologically confirmed Hirschsprung's disease. The parents were interviewed and asked about their own health and that of their other children, their brothers and sisters, and their nephews and nieces. With the exception of 2 adult sisters of 1 patient and 5 adult sisters of another, all brothers and sisters of the "index" cases were examined clinically for abdominal distention and by plain films of the abdomen for dilatation of the colon. Barium enema studies were made in doubtful cases. The evidence obtained from this study supports a genetic determination of Hirschsprung's disease. The over-all chances of a male sibling being affected are about 1 in 5; those of a female sibling being affected are small.

The authors have now treated 37 cases of Hirschsprung's disease by rectosigmoidectomy (Lancet 1: 19, 1950. Abst. in Radiology 55: 781, 1950). There have been 3 deaths in the series, 2 under anesthesia and 1 from peritonitis. Two cases are too recent to be included. The remaining 32 children were in excellent

condition at the time of the report; in 30 the gain in weight had been adequate. Evacuations were regular and spontaneous in 31, in about half without laxatives. Only 3 patients complained of occasional abdominal distention. Two children in the entire series died in the neonatal period and 1 died after subtotal colectomy.

Pathological study of these 40 cases of Hirschsprung's disease confirmed the previously reported absence of intramural ganglion cells and the presence of abnormal nerve bundles in the terminal undilated segment of bowel. Over 90 per cent of the recorded cases showed pathological changes in the rectum and part or all of the sigmoid colon. Less than 10 per cent had extremely long abnormal segments which appear to be incompatible with life if untreated.

A case is presented which showed agenesis of both nerve fibers and ganglion cells of the intramural plexuses distal to the duodenojejunal junction, a hitherto unrecorded condition. Its possible relationship to Hirschsprung's disease is discussed.

Ten figures.

**Hirschsprung's Disease Associated with Anal Stenosis and Subhepatic Cecum.** Gordon J. Harmston. Rocky Mt. M. J. 48: 29-33, January 1951.

In a case of Hirschsprung's disease in an infant of fourteen months, due to anal stenosis, the associated anomaly of incomplete rotation of the cecum was found. In a review of the literature, the author was unable to discover any other instance of association of these two anomalies.

A barium enema study showed the ascending sigmoid loop rising high through the right pelvis, with the top of the loop beneath the liver. The descending sigmoid loop reached to the left iliac fossa, whence the descending colon extended to the splenic flexure. There it doubled upon itself and the barium flowed transversely across the abdomen to beneath the liver, where the ileum was observed to fill as it entered the cecum below and from the left. The superior edge of the cecum followed the exact course of the lower liver margin.

Following gradual stretching of the anal stenosis, the megacolon showed progressive improvement.

Six roentgenograms. ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**Case of Aneurysm with Compression of the Rectum.** J. Reboul and Chavoix. J. de radiol. et d'électrol. 32: 116, 1951. (In French)

A 60-year-old woman was hospitalized with crises of subocclusion and circulatory disturbances of the right lower extremity. A fixed, non tender mass was palpated in the right iliac fossa. A barium enema examination revealed an irregular, fixed compressed area in the rectosigmoid area. Extrinsic inflammatory and neoplastic conditions were considered in the differential diagnosis. At operation a large iliac aneurysm was found adherent to the rectum.

One roentgenogram. CHARLES M. NICE, M.D.  
University of Minnesota

**Roentgen Diagnosis of Intra-abdominal Hernia.** A. Justin Williams and Fred L. Hewes. California Med. 74: 22-28, January 1951.

Nine possible fossae in the duodenojejunal region were described by Moynihan, in 1899, as potential sites



for small bowel herniation. Intra-abdominal hernias and torsion of loops of small bowel may be similar symptomatically and in their roentgenographic appearance. Other confusing possibilities are a congenitally short mesentery, congenital malrotation of the small bowel, and masses of small bowel matted together by adhesions.

In intra-abdominal hernia a length of small bowel is found "clumped as if confined in a sac" (Golden). This is in most instances better demonstrated in the erect position. The loops usually cannot be separated but may sometimes be moved *in toto* by external pressure. Barium meal studies of the small bowel must be performed, since these conditions are not usually shown on the plain film. Both erect and supine fluoroscopy are indicated. The possibility of reduction of the hernia during examination is to be considered. This may also happen between diagnosis and the time of surgery. Examination is better conducted during an acute stage in the clinical picture, since the hernia or torsion may be intermittently relieved.

The authors present 8 cases in which a preoperative diagnosis of intra-abdominal hernia was made. Spontaneous reduction occurred in 2 of these prior to surgery. In these 2 cases, however, operation revealed a damaged length of small bowel in a segment corresponding anatomically to the site of the herniation seen on the roentgen study. Of the other patients, only 3 were proved surgically to have intra-abdominal hernia.

Twelve roentgenograms.

JOHN F. RIESSER, M.D.  
The Henry Ford Hospital

**Floating Gallbladder Stones.** Edward C. Elsey and Donald L. Jacobs. *Am. J. Roentgenol.* 65: 73-76, January 1951.

Small transparent stones floating in the bile at various levels present not too rare a condition. These stones may not be visible with the patient supine, but will layer out if the upright position is assumed. Whether such floating stones are due to the artificial conditions of cholecystography, namely the presence of dye, or whether small cholesterol stones can float in concentrated native bile has been a subject of some discussion. Akerlund determined the specific gravity of bile of varying concentrations, examining the stones before they were dried by air. The specific gravity of even the smallest and lightest cholesterol stones was 1.040, which is the greatest specific gravity that native bile ever reaches. He concluded, therefore, that stones could hardly float in native bile unless its specific gravity were increased by the addition of gallbladder dye.

Two cases are presented illustrating the phenomenon of "floating stones."

Seven roentgenograms. DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Direct Radiographic Visualization of the Pancreas.** N. Macarini and L. Oliva. *Inform. med. Genova* 5: 29 ff., 1951. (In Italian)

By utilizing retroperitoneal insufflation of oxygen, by distending the stomach with gas, and by taking laminagraphs in the sagittal plane and in the horizontal plane, with the technic described by Vallebona (see *Radiology* 55: 271, 1950), the authors offer for the first time the opportunity of studying a normal pan-

creas by radiographic means. In spite of the fact that the reproduction of their films is rather poor, this work may well represent the beginning of a new phase in the study of this area, which has been up to now radiologically silent. It is hoped that the authors will pursue their work and give us a study of the pathological pancreas by their ingenious technic.

Twenty-one roentgenograms; 3 photographs.

CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Mediastinal Pseudocyst of the Pancreas. Case Report and Discussion.** Philip Edlin. *Gastroenterology* 17: 96-102, January 1951.

This is believed to be the first case of pancreatic pseudocyst located in the mediastinum to be reported. A 60-year-old Negro had a past history of abdominal pain recurring over many years, and diabetes mellitus for eight years. Five months prior to final hospital admission he had dyspnea, ankle edema, and x-ray evidence of a small left pleural effusion. Shortly before death a large mediastinal mass was demonstrated roentgenologically through the heart shadow. Autopsy revealed a large cystic mass in the posterior mediastinum which passed through the esophageal hiatus into the abdomen to the superior border of the pancreas, and filled the lesser peritoneal sac. No pancreatic tissue was identified in the cyst. Similar pseudocysts and chronic pancreatitis were found in the pancreas.

Pancreatic pseudocysts are thought to be caused by direct trauma, acute or chronic pancreatitis, and cholecystitis. In any case there is acinar damage with escape of pancreatic enzymes, gland necrosis, and formation of pseudocysts encapsulated by fibrous tissue. The pseudocyst is difficult to differentiate from the true pancreatic cyst, since either may have an epithelial lining, although this is more commonly found in the true cyst. The amount of fluid in the pseudocysts varies greatly, but it usually contains starch-splitting enzymes. Intrathoracic complications of abdominal pseudocysts of the pancreas are not rare. Left-sided pleural effusion is the most frequent, but elevation of the left diaphragm, disk atelectasis, pneumonia, empyema, and occasionally chylothorax may be present.

Two roentgenograms; 1 photograph.

DAVID A. HUOT, M.D.  
Pittsburgh, Penna.

#### DIAPHRAGMATIC HERNIA

**Pneumoperitoneum in the Differential Diagnosis of Diaphragmatic Hernia.** Richard C. Clay and C. Rollins Hanlon. *J. Thoracic Surg.* 21: 57-70, January 1951.

The authors report 4 cases in which pneumoperitoneum was useful in the diagnosis of diaphragmatic hernia simulating an intrathoracic tumor or cyst. This procedure is less hazardous, less expensive and more convenient than thoracotomy.

With local anesthesia, 300 c.c. of air are gently introduced 2 inches below and to the left of the umbilicus. Precautions are taken to avoid air embolism, which is the only serious risk. The reports bear out strongly the diagnostic importance of lateral as well as postero-anterior chest views both before and after the pneumoperitoneum.

Other diagnostic uses of the method are: outlining

pelvic organs, locating subphrenic abscess, distinguishing hepatic abscess from nodular cirrhosis, and differentiating suprahepatic from subhepatic inflammation.

Sixteen roentgenograms; 3 drawings.

DONALD DE F. BAUER, M.D.  
St. Paul, Minn.

**The Short Esophagus.** F. Soricelli and L. Di Guglielmo. *Arch. radiol.* 26: 212-228, 1950. (In Italian)

The authors report two cases of short esophagus with diaphragmatic hernia, one in a child three years of age and the other in a man sixty years old. The first case was uncomplicated and gave few symptoms. The second case was accompanied by epigastric pain and a severe anemia. X-ray examination in this case showed not only the short esophagus and the diaphragmatic hernia, but also a large ulcer crater along the lesser curvature just below the esophageal opening.

The authors review the literature on short esophagus, discuss the pathogenesis and embryology, and divide the cases into two classes. The first class includes those cases in which the condition is clearly of congenital origin. The second class includes those in which the esophagus has been shortened by scarring caused by pathological processes. The two cases reported are representative of these two types. The first was congenital; in the second shortening was attributable to long-standing ulceration.

Six roentgenograms; 3 drawings.

CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Traumatic Diaphragmatic Hernia.** B. Noland Carter, Jerome Giusefi, and Benjamin Felson. *Am. J. Roentgenol.* 65: 56-71, January 1951.

Traumatic diaphragmatic hernias arise as the result of direct or indirect trauma to the diaphragm. They have been classified into three main categories: (1) those caused by stab wounds; (2) those caused by gun shot wounds; (3) those caused by indirect violence, such as falls, crushing injuries, and steering wheel accidents; (4) those arising postoperatively from incision of the diaphragm. The condition may be recognized at the time of injury, during an interval stage, or after obstruction or strangulation has ensued.

In general, the diagnosis of traumatic diaphragmatic hernia may be readily made by roentgenologic examination. The most significant findings are: (1) an arch-like shadow resembling an abnormally high diaphragm; (2) extraneous shadows, such as gas bubbles, homogeneous densities, or other abnormal markings extending above the anticipated level of the normal diaphragm; (3) shift of the heart and mediastinal structures to the right; and (4) disk- or plate-like areas of atelectasis in the lung superjacent to the arch-like shadow. When the possibility of hernia is suggested by one or more of these features, the diagnosis can be established conclusively by roentgenoscopy of the thorax and studies with barium, orally or by enema, or both. The demonstration of obstruction or constriction of the stomach or colon as it passes through the torn diaphragm well below the arch-like superior border of the herniated viscus, will enable one to differentiate this condition from an eventration of the diaphragm or a subphrenic abscess. Free pleural fluid

which has become trapped at the base of the thorax may resemble diaphragmatic hernia but can be differentiated by means of a recumbent film of the thorax, which will show the fluid distributed over the entire thorax and the diaphragm in its normal position.

The repair of traumatic diaphragmatic hernia is best accomplished through a thoracic approach with an abdominal extension when greater exposure is required.

Eleven cases are reported.

Ten roentgenograms; 2 diagrams.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

## THE MUSCULOSKELETAL SYSTEM

**Giant-Cell Tumor of Bone. Current Status of Problems in Diagnosis and Treatment.** Louis Lichtenstein. *J. Bone & Joint Surg.* 33-A: 143-150, January 1951.

The author asserts that until there is general agreement in actual practice as well as theory as to what constitutes giant-cell tumor, it would seem to be futile to discuss results of treatment by one method or another. He attempts in this paper to dispel some of the current confusion by outlining certain pertinent advances of the past decade concerning the clinical and pathological features of genuine giant-cell tumor and of certain lesions that are frequently mistaken for it. Particularly he stresses the importance of separating from true giant-cell tumors some of the so-called "variants" which resemble it but are definitely different. Among the conditions which have been recognized as distinct entities are non-osteogenic fibroma of bone, chondroblastoma of bone, aneurysmal bone cysts, and the so-called giant-cell tumors of synovial or tenosynovial tissues, better known as pigmented villonodular synovitis, bursitis, and tenosynovitis.

The genuine giant-cell tumor is seldom observed in patients below the age of twenty and is usually situated in a long bone, involving the end of the bone. Very frequently trabeculated tumors with a soap-bubble appearance in the flat bones of the pelvis and shoulder girdle, and particularly in the vertebrae, are called giant-cell tumors, but actually these are probably aneurysmal bone cysts.

It is the author's impression that, given a sizable group of proved giant-cell tumors, approximately one-half are likely to have a favorable outcome if properly treated by whatever method, approximately one-third are likely to prove more aggressive and recur after treatment, while the remaining 15 per cent, more or less, will be frankly malignant and prone to metastasize to the lungs. An occasional giant-cell tumor will be found to be malignant at the time of initial tissue examination, but more often one has to reckon with malignant change incidental to one or more local recurrences.

In regard to therapy generally, the first step should always be adequate biopsy. Next one should decide as to whether or not the primary mode of approach should be surgical or radiotherapeutic. The author is inclined to favor the surgical approach, even though curettage is the most that can be done. No large series of giant-cell tumors treated by roentgen irradiation, with adequate follow-up, could be found, but reports indicate that, when radiotherapy is employed,

as small a roentgen dosage as possible should be utilized. The treatment of recurrences remains a moot question.

Finally, it is suggested that registry be established so that some conclusive opinion can be formed as to the proper mode of approach to giant-cell tumors. In that way an adequate check upon the pathologic diagnoses can be made and careful analysis of the therapy carried out on unquestionably proved cases.

I. MESCHAN, M.D.

University of Arkansas

**Osteoid Osteoma. A Clinicopathologic Study of 20 Cases.** Malcolm B. Dockerty, Ralph K. Ghormley, and Alfred E. Jackson. *Ann. Surg.* **133**: 77-89, January 1951.

The authors surveyed all cases at the Mayo Clinic in which the diagnosis of "sclerosing osteitis," "Brodie's abscess," "solitary cortical abscess," "localized osteitis fibrosa," "osteofibroma," "osteoma," and "osteoid osteoma" had been made. Roentgen and microscopic evidence of osteoid osteoma was found in 20 of these cases. The femur and the tibia were involved in 15 cases, and the humerus, ulna, scapula and vertebrae in 5. Symptomatically, pain of a boring nature and progressive in character was a predominant finding.

Sometimes early roentgenograms revealed no abnormalities in the presence of typical clinical symptoms (5 patients). Eventually, however, all the affected bones showed evidence of periosteal proliferation. In the later films, in 19 of 20 cases, typical radiolucent zones measuring from 3 mm. to 2 cm. were seen. In 5 patients these zones contained irregular foci of calcification. In the one case in which the transverse process of a vertebra was involved, the entire bony structure had been destroyed and there was no surrounding bony sclerosis. In the other 19 cases, relatively extensive osteosclerosis was observed around the radiolucent nidus. The degree and extent of the sclerosis had no apparent fixed relation to the age of the lesion as measured in terms of clinical symptoms and signs. Calcification within the central nidus similarly was seen early and late in the clinical story.

The authors discuss the differential diagnosis and treatment as well as etiology of osteoid osteoma. They state that the true etiology remains obscure. Review of cases previously reported as solitary cortical abscesses reveals that from the standpoint of history, clinical findings, and roentgenograms, these cases could not be distinguished from the present cases of osteoid osteoma. This brought up the following questions: Are osteoid osteomas and solitary cortical abscesses two phases of an essentially similar process? Are they variants of a single process or two different lesions with similar clinical and roentgenographic pictures? In one case in the present series, there was what was considered a true neoplastic change. In another case with typical clinical and x-ray findings, but not operated upon, follow-up roentgenograms demonstrated eventual disappearance of the lesion.

The authors conclude that such observations as those above lead them to believe that they are dealing with a lesion which may at times show one type of pathologic picture and at other times a different picture.

Twelve roentgenograms; 8 photographs and photomicrographs; 4 tables.

I. R. BERGER, M.D.

University of Louisville

**Natural Course of Osteoid Osteoma.** Erik Moberg. *J. Bone & Joint Surg.* **33-A**: 166-170, January 1951.

As a result of a study of some histologically verified cases of osteoid osteoma, the author shows that in the development of the disease process the characteristic small central nidus may increase through further destruction until it may be larger than the cross section of the normal bone at the same point. This development takes place simultaneously with a progression in clinical symptoms, particularly night pain. The nidus develops continuously by invasion of normal or eburnated bone.

Two clinically and roentgenographically typical cases are cited as offering some presumptive evidence that spontaneous healing may occur (Moberg: *Arch. f. klin. Chir.* **202**: 553, 1941; Sherman: *J. Bone & Joint Surg.* **29**: 918, 1947). This development appears contradictory to the claim that the disease is caused by bone infarction, nor is it compatible with the generally accepted definition of a tumor. Since a histologic diagnosis is lacking in both of these cases, it is unfortunately impossible to evaluate further the author's assumption as to the natural healing process, namely that the special remodeling process in the nidus brought about by the disease ceases spontaneously as the osteoid bone changes to more normal bone with resulting gradual reduction of the reacting cortical bone mass.

Fourteen illustrations, including 9 roentgenograms.

I. MESCHAN, M.D.

University of Arkansas

**Eosinophilic Granuloma of Rib, with a Case Report.**

Harold A. Kipp and Edwin R. Fisher. *J. Thoracic Surg.* **21**: 24-29, January 1951.

The sudden onset of left-sided chest pain, followed by the development of a lump, led to the surgical removal, from a 22-year-old woman, of a monostotic eosinophilic granuloma. Roentgenograms demonstrated an oval, sharply demarcated, osteolytic lesion of the ninth left rib in the axillary line. The medulla and outer cortex were affected. The inner cortex was spared. These observations were confirmed by the pathology report. There was no visceral involvement. No other bones were affected.

Clinical differentiation from Ewing's sarcoma of bone, myeloma, reticulum-cell sarcoma, Brodie's abscess, metastatic carcinoma, and simple bone cyst is considered difficult, and reliance is placed upon histologic rather than radiographic examination.

Four illustrations, including 1 roentgenogram.

DONALD DE F. BAUER, M.D.

St. Paul, Minn.

**Skeletal and Periarticular Manifestations of Hypervitaminosis D.** William R. Christensen, Charles Liebman, and Merrill C. Sosman. *Am. J. Roentgenol.* **65**: 27-39, January 1951.

The authors presented 5 cases which displayed unusual skeletal and periarticular manifestations of hypervitaminosis D.

Ingestion of excessive amounts of vitamin D<sub>2</sub> (irradiated ergosterol) may lead to the development of a roentgenologic picture characterized by concomitant occurrence of generalized osteoporosis and metastatic calcification. Abnormal calcium deposits may occur in almost any organ and tissue; however, under

certain circumstances they may appear as large, smoothly lobulated, amorphous, cystic masses confined to periarticular structures, namely bursae, synovial cavities and tendon sheaths. Metastatic calcification occurring in the absence of destructive bone lesions but in the presence of generalized osteoporosis should suggest the possibility of hypervitaminosis D<sub>2</sub>. In instances where the above criteria are met and metastatic calcification occurs in amorphous, smoothly lobulated masses confined to periarticular structures the differential possibilities are almost completely limited to chronic nephritis, hyperparathyroidism, and hypervitaminosis D<sub>2</sub>. The pathological physiology of hypervitaminosis D, as proved by animal experimentation, is closely duplicated by the findings in the cases presented. It is suggested that more attention be directed toward the possible specificity of vitamin D<sub>2</sub> in producing the clinical syndrome of hypervitaminosis D.

Ten roentgenograms.

[This paper is preceded by one by Caffey on Chronic Poisoning Due to Excess of Vitamin A (pp. 12-26), reprinted from *Pediatrics* 5: 672, 1950 (Abst. in *Radiology* 56: 304, 1951).] DANIEL WILNER, M.D.

Atlantic City, N. J.

**Traumatic Periostitis in Young Children.** George H. Barmeyer, Lee R. Alderson, and Walter B. Cox. *J. Pediat.* 38: 184-190, February 1951.

A common pediatric occurrence, the "acute limping leg" of early childhood, is frequently due to a traumatic periostitis of the tibia or femur, usually the result of some trivial, indirect injury associated with daily activity. The usual age of the child is one or two years, though the condition occurs also in the newborn infant.

Roentgenograms at the time of injury usually show no evidence of disease. Seven to ten days later some subperiosteal calcification is frequently demonstrable. No lamellation is noted, and the bony cortex appears normal. The tibia is most frequently involved, but occasionally the same process is seen in the femur.

Five cases of traumatic periostitis are presented in this article.

Four roentgenograms.

HOWARD L. STEINBACH, M.D.  
University of California

**Traumatic Fracture in Cooley's Anemia.** Antonio Toti. *Ann. radiol. diag.* 23: 81-92, 1951. (In Italian)

The author reports two cases of Cooley's anemia in which fractures of the forearm occurred following trauma. The formation of callus and the time of healing were found to be well within normal limits, showing that there is no impairment of the healing process in this condition. This observation is held to support the theory of a secondary origin of the bony changes in Cooley's anemia.

Fourteen roentgenograms.

CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Coccidioidomycosis and Tuberculosis in the Same Bones. A Case Report.** Charles G. Fraser, Stanley E. Monroe and James E. O'Hare. *Ann. Surg.* 133: 116-122, January 1951.

A 52-year-old white male gave a history of pulmonary tuberculosis since 1934, with treatment in 1945-47.

He was again undergoing treatment for the disease in 1948, when swelling, redness, and pain occurred in the right foot, particularly over the lateral aspect of the calcaneus. Subsequently, this area broke down and formed a draining sinus and soft-tissue abscess. In January 1949, a similar process developed in the opposite ankle. Cultures from this wound showed tubercle bacilli on two occasions. Later, biopsies of the soft tissues and curettings from the calcaneus and tibia showed granulation tissue and the presence of spheroid bodies of *Coccidioides immitis*. Roentgenograms of the right calcaneus in November 1948 showed an area of multilocular cystic formation, 5 cm. in diameter, with little or no surrounding bone reaction. In January 1949, the left tibia showed marginal erosion with destruction of the cortex of the distal end. Streptomycin therapy was instituted in November 1948, and at the end of two courses of treatment, cultures were negative for tuberculosis. In March 1949, a similar destructive process began in the distal left femur; however, the lesion did not progress and the area never became inflamed and did not break down.

The authors discuss coccidioidomycosis from the point of view of epidemiology and clinical findings, with special consideration of the changes and types of lesions seen in bone.

Three roentgenograms; 2 photographs; 2 photomicrographs.

WILLIAM H. SMITH, M.D.  
University of Louisville

**Adolescent Deficiency Disease. Report of a Case** Jarvis M. Smith. *J. Bone & Joint Surg.* 33-A: 230-234, January 1951.

The author reports the case of a white girl, age 13, who had every appearance of rickets or a rickets-like disease clinically, histologically, and by blood chemistry studies. The radiographic appearances of several of the bones were also consistent with rickets. Renal disease, primary hyperthyroidism, and other related illnesses were eliminated.

The patient was placed on high dosage of vitamin D, vitamin A, vitamin C, and various portions of the vitamin B complex. The response to this therapy was dramatic and rapid, and subsequent roentgenograms showed increased calcification in previous areas of rarefaction. Because of continued normal reports and maintenance of clinical recovery, the medication was discontinued and thus far the patient has remained completely symptom-free and normal in all respects.

Four roentgenograms.

I. MESCHAN, M.D.  
University of Arkansas

**Roentgen Diagnosis of Spondylolysis.** A. Wyss. *Schweiz. med. Wchnschr.* 80: 1257-1258, Nov. 25, 1950. (In German)

Spondylolysis is a minimal anterior dislocation of the 4th and 5th lumbar vertebrae which can be detected only in oblique views of the lower spine. The condition is due to a slit formation of the posterior arches. According to the literature this anomaly is present in 4 to 6 per cent of all spines, but in only 0.5 per cent does it give rise to lower back pain.

In the reading of oblique views of the lumbar spine, an imaginary line of demarcation has been helpful in determining even the smallest degree of anterior sliding of a vertebral body. The edge of a cardboard or ruler is placed in a vertical position at the posterior



border of the 3rd, 4th, and 5th intervertebral articulations consecutively. Under normal conditions the caudal joint should fall anterior to this vertical line. If it coincides or lies posteriorly, isthmus defects are present in most of the cases.

The contours of the interarticular portions are then studied. Normally the posterior joint surface should follow a curved line leading directly to the transverse process of the vertebra above. If this does not take place, a dehiscence is present, caused by the slit in the arch. It is then possible to determine the size of the slit by comparison with the interarticular joints above and below.

Two roentgenograms.

EUGENE F. LUTTERBECK, M.D.  
Chicago, Ill.

**Congenital Absence of the Sacrum and Coccyx. Report of Two Cases.** Vincent Del Duca, E. Vernon Davis, and James N. Barroway. *J. Bone & Joint Surg.* 33-A: 248-253, January 1951.

The authors report two cases of congenital absence of the sacrum and coccyx, known as sacrococcygeal agenesis, which when added to those cases hitherto reported in the literature bring the total to 47. The features manifested by these two cases were almost identical, the difference in development being due to the age variation of three years.

Absence of the spinal column below the lumbar region results in obvious narrowing of the pelvis and shortening of the intergluteal fold. Atrophy and dimpling of the buttocks are prominent manifestations, probably due to fibrous tissue contraction. The muscles of the lower extremities show evidence of atrophy which becomes increasingly prominent as skeletal growth progresses. Clubfoot is a frequent accompaniment. Although the illness is readily diagnosed radiographically the authors claim that the physical features should make the condition easily recognizable without roentgenograms. They speculate as to the possible embryologic etiology, but no definite conclusions are drawn.

Eight roentgenograms; 4 photographs.

I. MESCHAN, M.D.  
University of Arkansas

**Tuberculosis of the Sacro-iliac Joint. A Review of Seventy-five Cases.** Stanley T. Soholt. *J. Bone & Joint Surg.* 33-A: 119-130, January 1951.

The author presents data from a review of 75 cases of tuberculosis of the sacroiliac joint, and compares his observations with a previous series reported by Seddon and Strange (*Brit. J. Surg.* 28: 193, 1940). The patients were seen during the twenty-three-year period 1925-48. Each case had what was regarded as roentgenographic evidence of sacroiliac tuberculosis and 60 had positive bacteriological or pathological proof of the disease, or both.

An important feature of the disease is that it occurs primarily in young adults and is thereby distinguished from all other forms of joint tuberculosis. Eighty-three per cent of the author's patients had tuberculosis elsewhere in the body as well. In 47 per cent there were two or more other associated tuberculous lesions; 47 per cent also had associated skeletal lesions. The most common site was the spine and the next most common was the hip.

Pain was the first symptom in 83 per cent of the cases. The formation of an abscess during the course of the disease occurred in 79 per cent. Usually the abscess was directly over the sacroiliac joint; the second most common site was the inguinal region. Draining sinuses were almost universal following such abscess formation (2 exceptions).

The early roentgenographic findings are haziness or loss of definition of the joint line and irregularity of the articular surfaces with areas of erosion. If the disease progresses, bone destruction becomes more marked and cavitation may develop. Later there are bony ankylosis of the involved sacroiliac joint and increased density about the joint. Occasionally there is increased density about the joint without osseous fusion.

The prognosis is poor. In the present series 33 per cent of the patients died in the hospital and hospitalization was lengthy. Seventeen of the 25 patients who died in the hospital succumbed to overwhelming infection, amyloidosis, and inanition due to long-standing infection. Four died of tuberculous meningitis; 3 of severe pulmonary tuberculosis; and 1 of uremia.

The highest mortality rate is ordinarily found among the older patients. In the present series, however, the distribution of death very closely paralleled the age incidence of the disease. The average length of time from the onset of symptoms until death was thirty-eight months. It would appear that a draining sinus makes the prognosis more grave.

Sacroiliac tuberculosis must be treated as a manifestation of a systemic process. Bed rest, good nutrition, adequate immobilization in plaster, along with chemotherapy, are the most important therapeutic adjuncts. Streptomycin yields some encouraging results, but the follow-up period has not been long enough in the cases in which it has been employed for complete evaluation.

The efficacy of operative fusion in sacroiliac tuberculosis is still a matter of debate, and the author's findings do little to help settle the question. The data, however, suggest that this measure is of value in hastening the desired end-result of bony ankylosis in the involved joint.

Six roentgenograms; 2 charts; 6 tables.

I. MESCHAN, M.D.  
University of Arkansas

**Late Results in Legg-Perthes Disease.** Eugene R. Mindell and Mary S. Sherman. *J. Bone & Joint Surg.* 33-A: 1-23, January 1951.

The authors undertook the present study of patients with Legg-Perthes disease in an attempt to evaluate treatment in terms of end-results. The study involved 72 patients with 78 involved hips. Half of these were followed for six to fifteen years. Six patients were followed for over twenty-five years. In two-thirds of the cases growth at the upper end of the femur had been completed.

The therapy was classified as ambulatory and non-ambulatory. Ambulatory treatment refers to the use of crutches without weight-bearing or in some cases to an ischial weight-bearing brace. Non-ambulatory treatment includes prolonged periods of bed rest, traction, or immobilization.

Patients were considered to have a satisfactory result who were symptom-free, though on careful examination a few degrees of limitation of rotation or abduction and slight muscular atrophy were usually found. Roent-

genographic examination showed the hips to be without deformity and the articular cortices to be free of irregularities.

Those patients were classified as having fair results who had a few minor complaints, 1 or 2 cm. of shortening of the involved limb, and mild atrophy of the gluteal, thigh, and calf muscles. Roentgenograms showed a moderate flattening and widening of the femoral head and slight irregularity of the cortices of the femoral head, with or without associated acetabular changes, and a widened, shortened femoral neck with or without angulation.

The patients with poor final results had more pain, limp, and disability, as much as 4 cm. shortening, and considerable muscular atrophy. Roentgenograms demonstrated gross deformity of the femoral head and neck and occasionally of the acetabulum. Sclerosis, loose bodies, unreplaced and ununited fragments, or exostoses were sometimes present.

The poorest results were seen among the 13 patients who were untreated, only 3 of whom had a satisfactory outcome. No significant difference was demonstrated in the results following the use of ambulatory and non-ambulatory methods of treatment. Both methods produced a high percentage of good results. There were no differences among the ambulatory patients using crutches and those treated by braces. The younger the patient the better the prognosis.

It seemed in this series that extensive changes in the femoral neck generally indicated a poor prognosis. Asymmetrical growth retardation or epiphyseal arrest was another factor which contributed to the development of deformity. In the patients who obtained the best results, the epiphyseal cartilage plate always appeared to be normal and did not undergo premature closure.

The authors conclude that, inasmuch as no significant difference is found in results from non-ambulatory and ambulatory methods of treatment, the ambulatory method is preferable when the disease is unilateral. This avoids complications from prolonged bed rest and immobilization.

Fifty-two roentgenograms; 4 tables.

I. MESCHAN, M.D.  
University of Arkansas

**Hemoptysis Due to Elimination, by Way of a Bronchus, of an Osseous Fragment in the Course of Osteomyelitis of the First Rib.** André Meyer, Olivier Monod, J. P. Nico, and J. Chrétien. *J. franç. méd. et chir. thorac.* 5: 77-82, 1951. (In French)

A 26-year-old mechanic was admitted with his first episode of hemoptysis. At that time an opacity was noted in the apex of the left lung. Two months later a second episode of hemoptysis was followed by coughing up a fragment of bone. A roentgenogram showed a disturbance of the structure of the first rib on the left. Surgical excision disclosed osteomyelitis of the rib.

Three roentgenograms. CHARLES M. NICE, M.D.  
University of Minnesota

#### OBSTETRICS AND GYNECOLOGY

**Geometrics of the Pelvic Outlet.** H. C. H. Bull. *J. Obst. & Gynaec. Brit. Emp.* 58: 22-28, February 1951.

The author, with the help of an engineer, has con-

trived a geometric method for measuring the pelvic outlet. Assuming the fetal head to approximate in size a sphere 98 mm. in diameter, they sought to determine whether or not there would be room for such an unmolded head to pass through the outlet at term.

The radiographic data required for the purpose are the sacropubic length and the subpubic triangle. The sacropubic diameter is measured from the lateral view of the pelvis. It is the distance from the last piece of the sacrum to the midpoint of the interpubic diameter (obtained by drawing a line from the center point below the symphysis to the convexity of each ramus where it begins to turn backward and joining the point of contact of each line with the ramus). Correction to the actual length is made by any of the usual methods. The subpubic triangle is measured with a protractor from the interpubic and sacropubic diameters. It expresses the divergence of the rami and is of importance only in conjunction with the sacropubic diameter.

In the geometric method described here, the fetal head is represented by a succession of circles of 98 mm. diameter moving down the curve of Carus until the full diameter has passed the last piece of sacrum. Viewed from the front, the shape required for the passage of the head corresponds with the maximum chordal intersection of the occiput with the subpubic arch. The size of the chordal intersection varies with the curve of the subpubic arch and, as it varies, so also must the sacropubic length. From this, a series of parabolic curves has been developed for subpubic arches from 65 to 95 degrees, and on each curve a figure has been inscribed which is the length of the sacropubic diameter necessary for the passage of the head through the outlet for that particular angle. These curves are drawn on a transparency and superimposed directly on the film. From the curve which fits the arch the minimum sacropubic length necessary for passage of the head (without molding) can be read off. The author has also built a wooden model by which the geometric findings can be checked.

The method does not take into consideration molding, rocking at the sacroiliac joints, or the force of traction with forceps. The investigation has proceeded so far only for occipito-anterior position, and for geometric simplicity with a sphere of 98 mm. diameter.

Twelve illustrations, including 5 roentgenograms.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Uterovenous and Uterolymphatic Intravasation in Hysterosalpingography.** A. Drukman and S. Rozin. *J. Obst. & Gynaec. Brit. Emp.* 58: 73-78, February 1951.

The authors studied 62 cases of uterovenous or uterolymphatic intravasation, noted in the course of 2,000 hysterosalpingograms. Two distinct phenomena, intravasation and lymphatic transfer, were studied. The findings are summarized as follows:

The causes of venous intravasation cited in the literature, namely, excessive pressure, lesions of the uterine mucosa, and hysterosalpingography done shortly after menstruation or curettage, did not play a major role in the cases observed (12 cases = 18.7 per cent).

Intravasation under normal pressure, and with patent tubes, occurred under the following conditions, (a) in the presence of filling defects caused by a polyp or endometriosis (10 cases = 15.6 per cent); (b) in de-

formations of the uterine cavity due to myomata (23 cases = 36 per cent); (c) in cases with apparently normal uterus and patent tubes (habitual intravasation). On repetition of hysterosalpingography in patients of this last group intravasation always occurred at the same site (12 cases = 18.7 per cent).

The phenomenon of lymphatic transfer (7 cases = 11.0 per cent) is characterized by (a) closely reticular cloudy turbidity in the uterine wall; (b) slow clearing of oil from the uterine body, as differentiated from the rapid disappearance with venous intravasation; (c) accumulation of oil in the regional lymph nodes; (d) retention of lipiodol in the nodes for months and even years. No subjective complaints or complications were observed in lymphatic transigrations.

This article is very enlightening and should be read in the original by those interested in hysterosalpingography.

Fourteen roentgenograms.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

#### Oil Embolism During Hysterosalpingography.

Nathan Karshmer and William Stein. *Am. J. Obst. & Gynec.* 61: 458-460, February 1951.

The authors report a case of oil embolism occurring during hysterosalpingography performed with iodochloral. Fractional injections of 2 c.c. each, followed by films, had been performed until 6 c.c. had been given. At this time the right tube had not been visualized, and 5 c.c. more were injected in an effort to fill the tube or force it open. The patient felt nauseated and faint during the taking of the next film, which showed dye in the uterine plexus and left uterine vein, along with spilling into the peritoneal cavity.

The patient was symptom-free for a few days, following which fever and signs of pleurisy at the right base developed. Roentgenograms were interpreted as revealing a process compatible with pneumonitis or infarct. Within a period of three weeks the patient became normal clinically, and only a slight amount of residual pleural thickening in the right costophrenic angle was noticed in the roentgenogram. There was no evidence of opaque material in the blood vessels in a film of the abdomen taken about that time. No mention is made of iodized oil ever having been demonstrated in the lungs radiographically.

One roentgenogram.

T. FREDERICK WEILAND, M.D.  
Jefferson Medical College

### GENITO-URINARY SYSTEM

**Radiographic-Anatomic Study of Vascular Abnormalities in Pathologic Kidneys.** Ivo Orlandini. *Ann. radiol. diag.* 23: 125-146, 1951. (In Italian)

This is a beautiful radiographic study of 50 pathological renal specimens in which the vessels were injected with radiopaque material. The author demonstrates numerous vascular abnormalities found in various renal conditions, and the stereoscopic radiographs give the reader a preview of what may become possible in the future when better media and technics may allow the routine study of the vascular system of the kidneys in the living subject.

Twenty-nine roentgenograms.

CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Urethral Diverticula in Paraplegics.** Virgil A. Pate, Jr., and R. Carl Bunts. *J. Urol.* 65: 108-125, January 1951.

A review of the literature revealed 197 cases of diverticula of the urethra in males and these are tabulated. The condition is found more commonly in females. The authors report 28 cases of acquired diverticula of the anterior urethra in paraplegic patients.

Most writers maintain that acquired diverticula of the anterior urethra develop on a basis of obstruction and/or destruction of the urethral wall by inflammation or trauma. Twenty-six of the 28 cases in this series gave a history of suburethral abscess following instrumentation.

Pathological study of the walls of the diverticula revealed squamous metaplasia with keratinization and abundant fibrous tissue. No normal urethral glands were present. The relationship of coexisting disease of the genito-urinary tract is difficult to evaluate in paraplegics. The authors feel that the presence of vesico-ureteral reflux is of importance. This, they attribute to prolonged infection of the intramural portion of the ureter, with a loss of the normal uretero-vesical valve action. Of 114 paraplegics studied by x-ray examination, 33 per cent showed evidence of reflux. Of the 28 patients with diverticula, 10 had reflux.

Diagnosis of urethral diverticulum is generally made by cystourethrogram. A mass in the perineum, particularly during micturition, is the most common finding. Frequency, dysuria, pyuria, incontinence, tenesmus, and persistent discharge may be present.

The treatment of choice is surgical excision of the diverticulum with extensive plastic repair and temporary diversion of the urinary stream. The authors point out that, due to the latent and active infection in paraplegic patients, healing may be poor.

Forty-three roentgenograms; 6 photographs and photomicrographs.

A. E. O'HARA, M.D.  
University of Pennsylvania

### THE BLOOD VESSELS

**Varicose Ulcer: A Study of the Deep Veins with Special Reference to Retrograde Venography.** H. E. Lockhart-Mummery and J. Hillyer Smitham. *Brit. J. Surg.* 38: 284-295, January 1951.

Varicose ulcers constitute a medical and economic problem of considerable magnitude. On the basis of their incidence in Denmark (Bauer: *Acta chir. Scand.* Suppl. 74, 1942), the authors estimate the number of cases in England as between 100,000 and 200,000, involving an annual expenditure for treatment of some £3,000,000.

Patients attending a "varicose vein clinic" are divided into three groups: (1) those with varicose veins with perfectly healthy skin in the lower extremities; (2) those with pigmentation, induration, and even ulceration of the leg; (3) those with both ulceration and varicose veins in the thigh and leg. As is clear from a consideration of these clinical types and a review of the literature, the cause of varicose ulcers is not to be sought solely in varicose veins. Probably the most important cause is previous thrombosis, though the extent to which this is responsible is disputed by various authors, as is the role of recanalization in the production of ulceration.

In order to throw further light on these controversial matters, the authors made venographic studies in some

30 patients. A conventional ascending venogram with the patient supine was first obtained, followed by a descending venogram, with injection of the medium into the femoral vein at the groin, with the patient as nearly erect as possible. [This second procedure, which is new, appears to offer information obtainable in no other manner. It may take some of the guess work out of venography as done conventionally.]

The normal ascending and descending appearances are described and illustrated and 7 abnormal cases are presented with reproductions of the venograms. It is concluded on the basis of these and other observations: (1) that after thrombosis of the deep veins of the leg recanalization (with destruction of valves) does occur in the majority of patients; (2) that the occurrence of previous thrombosis cannot be excluded either by the patient's history or by a venogram obtained by the ordinary technic; (3) that, on the whole, the development of intractable ulceration and serious symptoms after thrombosis is delayed until recanalization is far advanced; (4) that in cases showing induration and ulceration where previous thrombosis has not occurred, similar femoral vein insufficiency with back-pressure can be demonstrated and is probably the causative factor; (5) that in patients with varicose veins in whom the skin of the lower leg is healthy, the femoral vein is normal or nearly so.

Three photographs; 19 venograms.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

#### TECHNIC; CONTRAST MEDIA

**Roentgen Diagnosis of Upper Abdominal Retroperitoneal Space-Occupying Lesions.** Archie Sheinmel and Edward A. Mednick. *Am. J. Roentgenol.* 65: 77-92, January 1951.

The authors made use of the normal mobility of the barium-filled stomach with changes in body position to evaluate alterations in volume of the epigastric, retrogastric, and retroperitoneal structures. To establish a standard for retrogastric measurements, normal barium-filled stomachs were examined roentgenographically in the right lateral recumbent and left lateral upright positions for individuals of hyposthenic, sthenic, and hypersthenic habitus. Studies in the right lateral recumbent position disclosed extensive mobility of the cardia and pars media and less free mobility of the antrum. This mobility of the gastric segments was utilized to disclose the presence of space-occupying lesions high in the epigastric, midepigastric, and paravertebral regions. Left lateral upright roentgen studies were found to be valuable in demonstrating tumors of the tail of the pancreas and kidney, as well as splenic enlargement.

Eight cases are presented, emphasizing the value of establishing the normal retrogastric measurements and illustrating their application in the interpretation of alterations produced by disease.

Thirty-nine roentgenograms; 1 drawing; 6 tables.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Soft Tissue Radiography. Technical Aspects and Clinical Applications in the Examination of Limbs.** Arne Frantzell. *Acta radiol. Supplement* 85, 1951.

This publication, from the Roentgen Clinic of the University of Upsala, consists of a thorough analysis

of the various technical factors involved in soft-tissue radiography, with examples of clinical possibilities of the method. The technic is that of Laurell.

The author begins with an analysis of the various factors which produce blur, viz., focal blur, screen blur, and motion blur. He states that effective blur is not equal to the numerical sum of the factors, but to the square root of the sum of the squared factors, viz.,  $(a^2 + b^2 + c^2)^{1/2}$ . The practical implication of this rule is that it is not worth while to reduce any one blur factor unless they are all equal. If they are not, the numerically largest one will be so dominant that it will be the only one worth reducing.

In analyzing focal blur, it was found that the focal image is not homogeneous, and photographs of various foci are reproduced illustrating this. In modern roentgen tubes the actual focal spot is linear, and focal blur is more accentuated toward the cathode and less toward the anode.

Intensifying screens cause some blur because of the relatively large size of the fluorescent crystals, and also because the crystals in the screen and the light-sensitive grains must be some distance apart. However, they do not give a visible graininess in the roentgen image. The distinct advantages of screens are that they shorten exposure time and that they increase photographic contrast. Intensifying factors and blur effect of various screens are compared in tables prepared by the author.

A simple method for estimating motion blur is illustrated.

Examples are given of the roentgen image of the cutis and subcutis in healthy and in edematous individuals. The reticulated pattern in the subcutis is discussed and the author concludes that it represents the loose connective tissue. Roentgen manifestations of subcutaneous edema are described and illustrated. The application of the method to studies of muscular tissue is discussed and exemplified by four cases of dystrophia musculorum progressiva.

Numerous illustrations, including 30 roentgenograms; 8 tables.

THOMAS F. ULRICH, M.D.  
The Henry Ford Hospital

**Relation between Tension and Exposure Times in Radiography.** A. Bierman and W. Hondius Boldingh. *Acta radiol.* 35: 22-26, January 1951.

The desirability of obtaining consistently reproducible densities in radiography is evident. With all other factors remaining constant (object, focus-film distance, film and screens, etc.), variations in radiographic densities are dependent upon variations in kilovoltage and milliamperage. Constant densities can be better achieved if the exact reciprocity of these factors can be clearly stated.

The authors have determined, experimentally, in the normal diagnostic range of 50 to 100 kv. that constant film densities are obtained, for practical purposes, when kv. and ma. are varied according to the formula  $k = ma. \times kv.$  Application of this relationship may then be substituted, with profit, for the old rule of thumb in current practice.

Four graphs.

JOHN F. RIESSER, M.D.  
The Henry Ford Hospital

**Properties of Fine-Grained Photographic Emulsions Used for Microradiography.** A. Engström and B. Lindström. *Acta radiol.* 35: 33-44, January 1951.

Employing radiation of 2.74 Å to 4 Å, produced by



a Machlett AEG 50T tube operating at 4.50 kv., the authors investigated the characteristics of fine-grained film emulsions, *vis.*, the Lippmann emulsion and Eastman spectroscopic plates 548-0 and 649.

Determination of density curves, resolving power, emulsion homogeneity, development artefacts and emulsion shrinkage permitted a comparison of the properties of these commercially available microradiographic emulsions.

Using these plates, a resolution of 1 micron can be obtained in recording images. Great variation was found in the homogeneity of emulsions, even in portions of the same plate. A very thin emulsion, permitting resolution of 0.5 micron, appears ideal.

Eleven figures; 2 tables. JOHN F. RIESSER, M.D.  
The Henry Ford Hospital

**Antihistaminic Drugs for Inhibiting Untoward Reactions to Injections of Contrast Medium.** Olle Olsson. *Acta radiol.* 35: 65-70, January 1951.

A solution called Dijodon D (20 mg. benadryl in 20 c.c. diodrast) was used in a controlled group of patients undergoing intravenous urography, and the incidence of allergic reactions compared with that for patients submitting to urography with diodrast alone. Significantly fewer and milder reactions were observed in the group receiving concomitant antihistamine therapy. All reactions, however, were not eliminated. This cannot be expected, since the entire gamut of allergic reactions is not adequately explained by histamine effect.

Three tables.

JOHN F. RIESSER, M.D.  
The Henry Ford Hospital

## RADIOTHERAPY

**Carcinoma of the Hypopharynx. A Clinical Study of 322 Cases, Treated at Radiumhemmet, from 1939 to 1947.** Folke Jacobsson. *Acta radiol.* 35: 1-21, January 1951.

Fractionated roentgen therapy is used at the Radiumhemmet in cases of carcinoma of the hypopharynx. For the 242 cases in the author's series treated more than five years ago, the five-year survival rate was 9.5 per cent; for the 84 cases in this group treated after the adoption of fluoroscopic beam direction, in 1943, the five-year rate was 14 per cent. It is suggested that a 20 per cent rate might be obtained with earlier diagnosis of lesions. The present series contained many large and far-advanced tumors. Best results, 17 per cent five-year survivals, were obtained in tumors of the lower hypopharynx, below the superior border of the cricoid cartilage.

A crossfire technic was employed with four narrow fields, two on each side of the neck. A tumor dose of 5,700 to 6,000 r in four weeks was found to be necessary for complete regression. Attempts to administer 6,600 r or more in a month resulted in fatal outcome in every instance. Teleradium is advocated for therapy of certain cervical metastases.

Physical characteristics of the tumor, degree of extension and general condition of the patient, as well as the reaction of the tumor and surrounding stroma, modify the course of therapy.

The complication of acute edema of the larynx demands maintenance of facilities for emergency tracheotomy. A point worthy of special note is the recognition of recurrence, in some cases after five to seven months, of the original symptoms and radiographic findings, which may indicate a late edematous reaction rather than regrowth of tumor. This phenomenon has been verified by direct endoscopy and, of course, definitely contraindicates another course of therapy which could be fatal. Institution of further therapy should follow only on biopsy confirmation.

Four figures; 7 tables. JOHN F. RIESSER, M.D.  
The Henry Ford Hospital

**Our Therapeutic Results in Irradiation of Malignant Goiter.** J. Šprindrich. *Acta radiol. et cancerol. bohemoslov.* 5: 2-7, 1951. (In French)

This study analyzes the results of radiotherapy in

68 cases of histologically proved carcinoma of the thyroid. In 42 cases thyroidectomy had already been performed; in 26 cases the patients were deemed inoperable. Irradiation was by means of a radium bomb at a distance of 6 cm. Three to five fields were utilized, with an average diameter of 6 cm. The dosage was 300 r per field to a total of 9,000 to 12,000 r measured on the skin in twenty-one to twenty-eight days. Of the 68 patients, 28 were alive three years after the treatments and 21 of these were clinically well. All of those who came for irradiation therapy directly after thyroidectomy are well. Those patients who first appeared for treatment with disseminated disease usually had a very poor prognosis. Five of 9 patients who had inoperable but localized disease were alive at the time of the report.

In 24 patients the malignant growth originated in nodular goiter which had been present from early life. The fact that so many of the patients came from regions of endemic goiter is suggestive of a close relationship between benign hypertrophy of the thyroid and the malignant lesion, and leads to the belief that prophylactic measures against endemic thyroid hyperplasia will result in a decrease in the number of patients suffering from thyroid carcinoma.

CHARLES M. NICE, M.D.  
University of Minnesota

**Radiation Therapy as an Adjunct to Surgery in Cancer of the Breast.** Benjamin F. Byrd, Jr. *Am. Practitioner* 2: 65-66, January 1951.

Granted that the use of irradiation as an adjunct to surgery in cancer of the breast is a controversial subject, little is gained by recording percentages and giving detailed analyses of a small number of cases. The author reports on only 40 cases treated by surgery and radiation, comparing these with 106 treated by surgery alone. No mention is made of how cases were selected. Axillary metastases were present in all. Although his own figures show a 28.8 per cent five-year survival rate for surgery alone as against 33.3 per cent with surgery plus radiation, he still reaches the conclusion that "there has been no significant improvement of the five-year survival rate by employing radiation as an adjunct to radical mastectomy."

Five tables.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**Neuroblastoma Sympatheticum with Metastases. Report of a Case with Apparent Recovery.** David Goldring. *J. Pediat.* 38: 231-234, February 1951.

Neuroblastoma is a highly malignant tumor that metastasizes early and widely. Although the prognosis is serious and reports of recovery are few, the condition is not always hopeless. The possible mechanisms of recovery are as follows: (1) The tumor may undergo spontaneous hemorrhage and necrosis and disappear. (2) It may undergo spontaneous maturation or metaplasia and become a benign ganglioneuroma. (3) It may be treated successfully by surgical removal followed by irradiation.

A case is reported in an infant with definite metastatic lesions in the liver, demonstrated during an exploratory laparotomy, and probable metastatic involvement of the right humerus and the skull. It was found impossible to remove the original tumor, which was located above the right kidney. The patient was given six deep x-ray treatments preoperatively to the right kidney region in divided doses of 200 r. An additional five treatments were given postoperatively for a total of 750 r. The physical factors are not stated.

The patient improved remarkably and was alive two years after the discovery of the tumor. At that time no abdominal mass was present and roentgenograms of the skeletal system revealed no metastases.

Two photomicrographs; 2 photographs.

HOWARD L. STEINBACH, M.D.  
University of California

**Carcinoma of the Bladder: Clinical, Therapeutic and Pathologic Aspects of 135 Cases.** Robert K. Royce and Lauren V. Ackerman. *J. Urol.* 65: 66-86, January 1951.

The authors reviewed 135 consecutive cases of carcinoma of the bladder, classifying the tumors according to their microscopic appearance. The transitional-cell carcinomas were divided into four groups: 38 were Grade 1, 23 Grade 2, 25 Grade 3, and 25 Grade 4. There were 11 undifferentiated carcinomas and 12 primarily squamous-cell carcinomas. One tumor was listed as an unclassified carcinoma.

Though the more malignant tumors tended to be larger than those of low-grade malignancy, the differentiation was not sufficient to be significant. A much closer relationship was demonstrated between the tumor size and prognosis. As a rule, the outlook for patients with the larger tumors was much less favorable than for those with smaller lesions. Seventy-five per cent of the transitional-cell and undifferentiated carcinomas were located on the base or neck of the bladder, in contrast to the squamous-cell carcinomas, which involved the dome and anterior bladder wall. Tumors in these latter locations had a poorer outcome than those located at the bladder base.

Ninety-four of the patients were males and 41 were females, and the average age was 60.8 years. The most common initial symptoms were hematuria, with or without pain, and dysuria not associated with hematuria. Painless hematuria was usually associated with tumors of low-grade malignancy and dysuria with tumors of high-grade malignancy.

Complete follow-ups were obtained in 104 cases (77 per cent). Twenty-eight per cent of these patients had a five-year survival, but the average survival period was two years and ten months. At one time or another,

most of the tumors were treated by several methods: endoscopic fulguration for tumors of Grades 1 and 2, cystotomy with local excision and fulguration for lesions considered too large to be destroyed endoscopically, partial cystectomy for tumors of rather high-grade malignancy, radon seed implantation following excision or fulguration, deep roentgen therapy for initially inoperable or incompletely removed tumors, and open roentgen therapy for far advanced cases which were otherwise considered hopeless. In general, treatment was satisfactory for tumors of low-grade malignancy and unsatisfactory for those of high-grade malignancy, regardless of the method used.

Fourteen photomicrographs; 1 diagram; 13 tables.

JOHN M. DENNIS, M.D.  
University of Pennsylvania

**Treatment of Malignant Tumors of the Testis.** David D. Merren, Samuel A. Vest, and Charles H. Lupton, Jr. *J. Urol.* 65: 128-135, January 1951.

The authors present a study of 67 cases of malignant tumors of the testis seen at the University of Virginia Hospital over the period 1921-49. In only 41 of these cases were sufficient clinical data available to include them in the series; of these 12 were seminomas and 15 embryonal carcinomas, according to the Friedman and Moore classification (*Mil. Surgeon* 99: 573, 1946). The remaining 14 tumors were of miscellaneous types, and no single type was sufficiently well represented to permit statistically significant figures on treatment results.

All the patients were treated with simple orchiectomy, and most received postoperative irradiation at 200 kv. [No further information is given concerning the irradiation.] Survival figures are given as follows: 53 per cent of the patients with embryonal carcinoma survived two to twenty-three years, and 67 per cent of the patients with seminoma were living at the time of the study, with one surviving 19 1/2 years.

It is concluded that the proper therapy for seminoma is simple orchiectomy plus postoperative irradiation, while the best therapy for embryonal carcinoma has not yet been determined. The suggestion is made that future writers on the subject adopt the Friedman and Moore classification so that results from various clinics can be compared on a common basis.

Seven photomicrographs; 4 tables.

W. C. OWSLEY, JR., M.D.  
University of Pennsylvania

**Soft Tissue Tumours: Their Natural History and Treatment.** Stanford Cade. *Proc. Roy. Soc. Med.* 44: 19-36, January 1951.

Soft-tissue sarcoma is a tumor of mesenchymal origin arising from the connective tissues of fasciae, muscles, tendons, tendon sheaths, intermuscular septa, and synovial membranes. A series of 153 such tumors, of which 146 were verified histologically, is presented. Terms such as spindle-cell sarcoma, neurogenic sarcoma, and myxosarcoma are without definitive meaning and their use is avoided by the author. Sarcoma of the viscera are not considered in this study.

The greatest incidence of soft-tissue sarcoma is in the third decade, but the tumor may occur at any age, even in the newborn. Tumors of the trunk and limbs occur more frequently in males, but in other sites no sex discrimination is exhibited. The most frequent

site is in the extremities, particularly the lower limbs which were involved in more than 50 per cent of the present series. Fortunately the prognosis is best in sarcomas of the extremities and trunk.

Fibrosarcoma, the most common type, is composed of spindle cells and is derived from fibroblasts. Multiple widespread metastases are common. Synovial sarcoma arises from synovial membranes of bursae, tendon sheaths, or joints, and has a less favorable prognosis. The more rare liposarcoma is composed of foamy immature fat cells and is characterized clinically by its rapid growth and great size. Rhabdomyosarcoma is derived from the myoblast and histologically contains an admixture of striated cells and ribbon-shaped myoblasts; the prognosis is extremely poor. Soft-tissue sarcomas with a predominant vascular structure are classified under the heading of angiosarcoma.

Local enucleation of these neoplasms proved to be a failure, because of recurrence. The management was by wide excision with pre- and postoperative radiation, by amputation with or without radiation, or by radiation alone. The results are given for 128 cases. Wide excision in combination with radiation yielded a survival rate of more than 60 per cent. The other two courses of treatment, usually utilized in more advanced cases, offered lower salvage rates. The longest survival in the series is twenty-six years. Radiation alone is advocated only when radical excision cannot be undertaken. In contrast to the radiation therapy of malignant epithelial neoplasms the author suggests that moderate doses of radiation over a long period may be the method of choice when this type of therapy is indicated for soft-tissue sarcoma.

One roentgenogram; 5 photographs; 6 photomicrographs; 13 tables.

EARL R. HAYNES, M.D.  
The Henry Ford Hospital

#### Lymphocytoma Cutis. Report of Two Cases.

Adolph B. Loveman and Maurice T. Fliegelman. *Arch. Dermat. & Syph.* 63: 169-181, February 1951.  
**Benign Solitary Lymphocytoma. Report of Three Cases.** Coleman Mopper and James R. Rogin. *Arch. Dermat. & Syph.* 63: 184-190, February 1951.

Lymphocytoma cutis is a rare benign skin condition of unknown origin presenting single and multiple papular lesions, usually on the face, which on biopsy show a dermal infiltration of cells of the lymphocyte series in a fine reticulum. Germinal centers may be present. The lesion, which may be circumscribed or diffuse, is separated from the epidermis by an uninvolved subepidermal layer of tissue and consists of small dark lymphocytes alone or in combination with larger reticulum cells having pale nuclei.

The appearance varies widely, causing confusion with many lesions such as rhinophyma, sebaceous cyst, tuberculosis cutis, tertiary syphilis, lipid dyscrasias, keloid, neurofibromatosis, Boeck's sarcoid, sarcoid of Spiegler-Fendt, lupus miliaris disseminatus, lupus erythematosus, epithelioma, dermoid cyst, lymphangioma, benign cystic epithelioma, follicular lymphoma, leukemia, and lymphosarcoma. The diagnosis is made by the histologic appearance associated with normal blood findings and no evidence of systemic disease over a period of years.

Superficial roentgen irradiation in doses of 300 to 400 r causes rapid regression, but recurrence is common. Arsenic and antibiotics are valueless.

Loveman and Fliegelman present two case reports. Their first patient was a young woman with a small, bluish, papular lesion on the nose which had recurred in scar tissue following earlier electrodesiccation. Many lesions had developed over a period of seven years and had been treated by electrodesiccation. During the period of observation, new lesions appeared on the nose, cheeks and ear lobes, the latter being a common site of involvement in this disease. Biopsies showed a dense accumulation of lymphocytes in the dermis, consisting of deep mature cells and larger pale cells with one or two nucleoli. Primitive germinal centers were seen.

Unfiltered superficial roentgen therapy in doses of 150 to 200 r given every two to three weeks for two or three doses caused rapid disappearance of the lesions, but recurrences as well as new lesions were common.

The second patient was a 64-year-old male with a painless enlargement of one side of the nose, which was spongy and presented telangiectasia and scarring, the latter being the result of electrodesiccation done four years earlier in the belief that the condition was rhinophyma. Biopsy showed a circumscribed mass of cells in the dermis, consisting of small dense lymphocytes as well as larger cells with pale-staining nuclei. X-ray therapy was given, similar to that used in the first case, with a satisfactory response. New lesions which appeared later on the left ear lobe, left temporal area, and left jaw responded to 150 r of unfiltered x-rays given three times with a three-week interval between treatments. Within a week after the first treatment the lesions had disappeared. They had not recurred on observation six months later.

Eight illustrations.

Mopper and Rogin report 3 cases of benign solitary lymphocytoma. They mention the belief of some investigators that follicular lymphoma, lymphocytoma cutis, and Spiegler-Fendt sarcoid may all be variants of lymphosarcoma.

The first patient was a 44-year-old male with a papular, spongy, painless lesion on the nose, histologically characteristic of lymphocytoma. Roentgen therapy was given for a dose of 345 r, in air (74 kv., 4 ma., and a filtration of 0.5 mm. Al), and by the tenth day the lesion had grossly regressed. The dose was then repeated, and two weeks later the tumor was gone. There had been no recurrence three and a half years later.

The second patient was a 55-year-old woman who had an elevated red area across the bridge of the nose which was spongy and painless. Biopsy established the diagnosis of lymphocytoma, and the patient was given 150 r, in air, with filtration of 0.5 mm. Al. One month later, the lesion had greatly regressed and the dose was repeated. Three months after this the tumor was gone. It had not recurred two and a half years later.

Mopper and Rogin's last case was that of a 30-year-old Negroess with a small spherical mass on the right upper eyelid, which was spongy and painless. On excision, the lesion proved to be lymphocytoma.

Two illustrations. CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

#### Treatment of Haemangiomas of Naevi with Thorium

X. R. E. Bowers. *Brit. M. J.* 1: 121-124, Jan. 20, 1951.

Hemangiomas may be divided into two types: (1)

the flat or port-wine stain, which is composed of dilated capillary vessels, and (2) the cavernous type, which is composed not only of dilated capillaries, but also of intercommunicating blood-filled spaces. The flat capillary port-wine stains are nearly always persistent, but the cavernous type is prone to disappear without treatment by the age of six.

The author studied a series of 48 cases treated since 1939 with thorium X, 44 of which he followed personally. Thorium X is a radioactive substance, which emits alpha particles. When painted on the skin in an alcoholic solution it has a penetrating power of only 0.2 to 0.3 mm. beneath the surface. Its half life is 3.64 days.

In the author's cases the erythema following application of the thorium X lasted about two weeks. After another week, the treatment was repeated, so that the patient received a treatment about once every three to four weeks. From 4 to 84 paintings were given over periods of a few months to several years.

The results were classed as "good" when the lesion disappeared; "moderate" when there was a marked fading; "bad" when there was little or no change. Of the results in 44 cases, 20 were classed as "good," 12 were "moderate," and 12 "bad." Out of the 20 "good" cases, however, it is the author's opinion that 13 patients would have had a spontaneous cure if nothing had been done. The age of the patient is apparently not a factor in the cure, as there were in the series of "good" results patients whose ages were 44, 40, 38, 13, and 10 years. The author's observations, also convinced him that it was of very little use to continue the paintings for more than ten treatments.

Pin-point cautery was used on 2 patients with good results. The author believes that carbon dioxide snow is difficult to control, is quite painful, and may leave some atrophy of the skin.

One table, giving details of the 44 cases.

JOSEPH T. DANZER, M.D.  
Oil City, Penna.

#### Renal Angioma: Suspected Bilateral Involvement.

Bernard E. Paletz and George Sewell. *J. Urol.* 65: 9-14, January 1951.

Renal hemangioma is a relatively rare condition, only 70 cases having been found in a recent review of the literature. In all cases reported, involvement of only one kidney has been mentioned. The authors' case presents two unusual features: first, strong evi-

dence that both kidneys were affected; second, cessation of hemorrhage following deep x-ray therapy.

The patient, a 21-year-old Negro male, gave a history of occasional hematuria (average of once yearly) of ten years duration and profuse bleeding for two days prior to admission. The hematuria persisted, and after ten days a right nephrectomy was performed. The pathological report was "hemangioma, multiple, diffuse right kidney." On the seventeenth postoperative day the patient again began to bleed, and the hematuria eventually became so alarming that, in an attempt to control it, deep x-ray therapy (tissue dose of 435 r) was given to the left kidney through two portals. Bleeding suddenly ceased approximately five weeks after treatment and had not recurred at the time of the report (eight months later).

Four illustrations. J. L. JARVIS, M.D.  
University of Pennsylvania

#### Problem of Pregnancy in Hodgkin's Disease.

René Gilbert. *Acta radiol.* 35: 71-75, January 1951.

The possible deleterious effect of pregnancy on the character and course of Hodgkin's disease has led some authorities to advocate indiscriminate therapeutic abortion in patients who become pregnant. The author believes that this view should be revised in the light of present knowledge of the disease and the results that have been attained. He has observed thirteen pregnancies in nine mothers since 1926. He concludes, with Papillon and Chavanne (*J. méd. Lyon* 31: 127, 1950), who studied 60 cases from the literature, including 12 of their own, that:

1. Pregnancy, in a period free from symptoms, has no influence whatsoever on Hodgkin's disease.

2. With the disease in an evolutive period, frequent relapses are seen during the first six months of gestation, or during the puerperium, but there is no marked influence on the course of the disease.

3. Hodgkin's disease, having appeared during pregnancy or the puerperium, nearly always results in a rapid, feverish course, responding poorly to roentgen therapy, with a short survival time (average less than eighteen months).

In the latter two situations the physician's clinical judgment as to the indications for abortion must prevail, but even the interruption of pregnancy, in the rapidly evolutive forms, is of little avail.

JOHN F. RIESSER, M.D.  
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## RADIOISOTOPES

#### Estimating Radioelements in Exposed Individuals.

Jack Schubert. I. Radioelement Metabolism. *Nucleonics* 8, No. 2: 13-28, February 1951. II. Radiation Dosage and Permissible Levels. 8, No. 3: 66-78, March 1951. III. Bioassay Operations and Procedures. 8, No. 4: 59-67, April 1951.

With an increasing number of workers handling radioactive materials, more data are needed on the fate of radioelements in the body. Based on considerable research covering physical chemistry and metabolic behavior of certain radioelements, this series of papers represents a thorough discussion of the theoretical and practical considerations involved.

It is so detailed and covers so many aspects of the

subject that it cannot be adequately abstracted and one is forced to recommend a reading in the original. The topics covered, however, can be briefly outlined.

Part I, which takes up the metabolic aspects, covers the following:

- A. Aspects of the solution chemistry of cationic radioelements.
- B. Mechanisms for interpreting metabolism.
  1. Cation exchange reactions.
  2. Ion exchange uptake by bone (a physical-chemical picture).
  3. Colloidal absorption uptake by bone.
- C. Rate of incorporation in bone.



- D. Blood disappearance.
- E. Soft-tissue deposition.
- F. Body elimination of radioelements.
- G. Metabolism after inhalation.
- H. Treatment of radioelement poisoning.

The practical side of judging the amounts and fate of radioactive substances that enter a worker's body involves consideration of arbitrary standards. These standards interrelate physiological data on "standard man" and the properties of radioelements most harmful to him. This phase of the problem is covered in Part II.

A certain amount of physiological and biochemical data on man is necessary in order to estimate probable distribution, excretion, and intake of radioelements. Further, the sensitivity of many analytical procedures may vary considerably depending upon the amount and kind of interfering substances that may be present in a given tissue or excreta. These factors are covered in tables setting forth the weights of the different organs, physiologic data, and the chemical composition of human tissues in the standard man.

The potential radiotoxicity of the elements is a complex function that involves the following factors:

- Radioactive or Physical
  - A. Half-life.
  - B. Energy and kind of radiations.
- Physiological and metabolic
  - A. Route of administration.
  - B. Rate of elimination.
  - C. Chemical properties and nature of the compound.
  - D. Degree of localization within the body.
  - E. Age and life expectancy of the individual.
  - F. Concentration administered.
  - G. Physical state of radioelements.

Other factors to be considered are the differential absorption ratio and the type of radiation—in other words, the effective energy absorbed. This also is tabulated for various radioelements. On top of all this, allowance must be made for man's background radiation. Permissible levels in the body and excreta are presented in tabular form, and specific information regarding numerous elements is supplied.

Based on established practices at the Argonne National Laboratory, Part III outlines recommendations for administrative and analytical procedures designed to safeguard personnel from over-exposure. Requirements for bioassay operations are as follows:

1. The bioassay laboratory should be isolated and have equipment, atmosphere, and fixtures as free as possible from contamination.
  2. Analytical methods should be capable of isolating carrier-free amounts of a radioelement from large amounts of urine and feces.
  3. The alpha-counting instruments should have a maximum background of five counts an hour for a sample counted at 50 per cent efficiency.
  4. Strict regulations for collecting and handling specimens from personnel should be put into effect.
- Topics covered in connection with bioassay operations and procedures are: laboratory facilities, ashing of samples, counting techniques, and analytical radiochemical procedures. These last are outlined for radium, plutonium, americium, curium, polonium, actinium, protactinium, thorium, yttrium and rare

earths, alkaline earths, tritium, sulfur, carbon, and radioisotope mixtures.

Administrative problems are discussed and a reproduction of the punch-card type of record is included.

A bibliography is appended to each of the three parts of this comprehensive discussion.

Eight illustrations; 15 tables.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Some Varied Applications of Radioactive Isotopes to the Localisation and Treatment of Tumours.** D. W. Smithers. *Acta radiol.* **35**: 49-61, January 1951.

This is a brief review of the initial applications of various radioactive isotopes, in tumor localization and therapy, at the Royal Cancer Hospital in London. It is not intended as a final assessment of their clinical worth, so that no real conclusions can be drawn from the presentation. However, it does point up some of the avenues of expansion now being followed in the field of radiotherapy.

Iodine<sup>131</sup>, phosphorus<sup>32</sup> and gold<sup>198</sup> have been utilized for tumor localization, depending upon their biochemical affinities. Gold<sup>198</sup>, in colloidal suspension, has been applied therapeutically by local infiltration and by intraperitoneal injection. Sodium<sup>24</sup> and bromine<sup>82</sup>, in latex bags, have been used for intracavitary application within the urinary bladder. The use of tantalum<sup>182</sup>, by interstitial implantation, and phosphorus<sup>32</sup>, in polythene as a surface applicator, is also demonstrated.

Three roentgenograms; 10 photographs and photomicrographs; 2 diagrams; 1 graph; 2 tables.

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**On the Possible Application of Isotopes to the Management of Cancer.** Simeon T. Cantir. *Ann. Int. Med.* **33**: 1450-1458, December 1950.

The application of isotopes to the cancer problem can be directed either toward the broad field of investigations concerning the etiology of neoplastic disease or toward therapeutics. The actual use of radioactive isotopes has thus far been limited. In the leukemias and in a few rare cancers of the thyroid gland a beginning has been made in applying the isotopes to treatment, but those neoplastic diseases responsible for the high cancer mortality (cancer of the gastro-intestinal tract, breast, uterus, lung, etc.) have not been touched.

The author reviews at length the biologic aspects of radiosensitivity and concludes that the degree of success in the application of ionizing radiations to cancer is dependent fundamentally upon the degree of radiosensitivity of the cells. One can hope to succeed only if the cancer is one which has a radiosensitivity greater or closely paralleling that of the normal tissues about it.

If a tumor is to be controlled, then *all* malignant cells must be sterilized, and this includes those on the periphery adjacent to vital structures. The problem, then, is how to avoid injury to normal and vital structures, yet adequately irradiate the tumor. The obstacle lies largely in the range of effective radiating energy of the radioactive isotope. Taking as an example tritium (H<sup>3</sup>), the author points out that its effective energy permeates tissues in dimensions of

microns, ideal as an intracellular radiator. Its half-life is long and, being hydrogen, it can expect to be incorporated into the molecular structure of most tissues. But to effect specific localization of tritium in malignant cells only and to cause its elimination from the body with safety once its cancericidal mission is accomplished remains a difficulty.

The question is raised: Will the use of the radioisotopes enlarge the scope of radiation therapy by applicability to a wider range of tumors? Radiation therapy is at present limited to a minority of cancers, since these are the only ones with a radiosensitivity favorable to this approach. No practical means is known to increase the inherent vulnerability of cells to radiation.

A further obstacle relates to selective deposition. Radioiodine is unique thus far in this respect. However, in most instances of thyroid cancer, the deposition in the cancer is less than that in the healthy gland. Radiophosphorus has not in any way altered the mortality from the lymphomas, for it is not selectively deposited within those malignant cells. It is deposited generally throughout diseased and healthy cells of a group of tissues and the limitation of its effectiveness is largely due to its non-selectivity among cells of the same tissue.

Other obstacles must be overcome. The carcinogenic properties of certain isotopes and newly discovered elements are well known. Already there is suggestive evidence that a higher rate of eventual leukemia among the group of polycythemia treated by  $P^{32}$  exists.

STEPHEN N. TAGER, M.D.  
Evansville, Ind.

**Radioiodine ( $I^{131}$ ) in the Diagnosis and Treatment of Diseases of the Thyroid.** Fenton Schaffner, Morris T. Friedell, and Irvin F. Hummon. *Illinois M. J.* 99: 15-21, January 1951.

Tracer doses of  $I^{131}$  ranging from 0.1 to 1.0 millicuries were administered orally to 58 patients with and without thyroid disease, and the uptake measured twenty-four hours later with a Geiger counter. The average uptake in patients with hypothyroidism was 9.8 per cent, in those with normal thyroid function 22.6 per cent, and in those with hyperthyroidism 51.8 per cent. In general an uptake of more than 30 per cent indicated hyperthyroidism.

Radioiodine was given to 25 patients for the treatment of various diseases of the thyroid. Excellent results were obtained in 18 of 21 cases of toxic goiter; hypothyroidism developed in 1 patient. One patient with a non-toxic goiter responded well to treatment. Three cases of thyroid carcinoma were unimproved.

Four figures; 3 tables.

**Lingual Thyroid: Use of Radioactive Iodine in Diagnosis.** John R. Timmons and James M. Timmons. *Ann. Surg.* 133: 90-94, January 1951.

The authors briefly review the subject of lingual thyroid and point out that, following surgical excision of this type of "aberrant thyroid gland," myxedema of varying degree of severity is a frequent complication. The occurrence of thyroid tissue on the tongue is dependent on non-migration of the thyroid anlage from the region of the foramen cecum during embryologic development.

Radioactive iodine in tracer dose quantities were

used in two cases in which nodules were found on the posterior aspect of the tongue, in an attempt to answer three questions:

- (1) Is this aberrant thyroid tissue?
- (2) Is there any thyroid tissue present in the normal pretracheal area?
- (3) Are symptoms sufficient to warrant excision of the lingual nodule?

In the first case presented the result of Geiger counter measurements led the authors to believe that all of the patient's thyroid glandular tissue was on the tongue. This patient did not elect to have surgery performed.

In the second case, the findings clearly disclosed thyroid tissue in the normal pretracheal region in addition to that present on the tongue. This patient was asymptomatic and removal of the lingual thyroid tissue was thought to be warranted.

I. R. BERGER, M.D.  
University of Louisville

**Treatment of Hyperthyroidism with Radioactive Iodine.** Gilbert B. Forbes and Anne M. Perley. *J. Pediat.* 38: 158-163, February 1951.

A case of diffuse toxic goiter in an 11-year-old girl is reported. Because she had rheumatic heart disease, it was decided to treat her with  $I^{131}$  rather than surgically. Five millicuries of the isotope were administered by mouth in a single dose. The basal metabolic rate dropped abruptly in the fifth week. During the sixth week, a decrease in restlessness, exophthalmos, and in tremor of the extremities was noted. After three months the patient exhibited no signs or symptoms of thyrotoxicosis other than persistence of mild hypertension and slight exophthalmos. The blood pressure was normal six months later.

The patient subsequently had a normal sexual development, with the menarche at twelve years.

Two graphs. HOWARD L. STEINBACH, M.D.  
University of California

**Inhibition of Uptake of Radioactive Phosphate by Human Erythrocytes in Vitro.** D. R. H. Gourley. *Am. J. Physiol.* 164: 213-220, January 1951.

It is demonstrated by the author that the rate at which  $P^{32}$  is taken up by human erythrocytes *in vitro* is depressed by the addition of iodoacetic acid or sodium fluoride. The inhibitory action of iodoacetic acid is not reversible and is exerted almost entirely upon the  $P^{32}$  uptake of the erythrocytes, rather than the white cells and platelets. The presence of higher concentrations of sodium fluoride brings about what appears to be a two-phase uptake of  $P^{32}$ . The initial phase is a process of rapid diffusion, the rate of which is not affected by a drop in temperature from 37 to 15° C., while the later phase is similar to the depressed chemical mechanism observed in the presence of iodoacetic acid. A combination of iodoacetic acid and sodium fluoride inhibits the  $P^{32}$  to a greater degree than the maximum observed with either of the two alone but does not cause complete inhibition. According to Wilbrandt's data (*Pflüger's Arch. f. d. ges. Physiol.* 243: 519, 1940), the glycolytic system of the erythrocytes is completely inhibited by the concentrations of these substances which have a maximal effect on  $P^{32}$  uptake. It is inferred that enzymatic reactions other than the phosphorylating reactions of glycolysis are involved in phosphate transfer in erythrocytes. Sodium azide,

2,4-dinitrophenol, cysteine, and mercuric chloride are without effect on  $P^{32}$  uptake.

Three charts; 2 tables.

**Testing Blood Plasma to Tissue Exchange Rate by Urine Isotope Ratio: Inorganic Phosphate.** Herbert D. Friedlander and Walter S. Wilde. *Am. J. Physiol.* **164**: 159-166, January 1951.

The isotope method of calculating the rate of transfer of substances from the blood plasma to tissues depends upon a precise measure of the ratio of the tagged and the non-tagged substances in the plasma which are actually physicochemically active in undergoing exchange. The authors have tested this by measuring the ratio of isotopes accumulated in the urine over a period and comparing it with the ratio of the isotopes in the plasma as averaged over time for the same period. Based upon measurements of the acid-soluble phosphate fraction in either system, urine receives two to five times the amount of tracer phosphate ( $P^{32}O_4$ ) predicted from the plasma ratio. Possible explanations are discussed. Calcium, based upon calculations of Govaerts (*Am. J. Physiol.* **159**: 542, 1949), yields the predicted ratio in urine.

Four graphs; 1 table.

**Uptake and Conversion of Radioactive Iodine ( $I^{131}$ ) by Thyroid Gland in Vivo and in Vitro in Tourniquet Shock in Rats.** Milton W. Hamolsky, Z. S. Gierlach, and H. Jensen. *Am. J. Physiol.* **164**: 35-43, January 1951.

An early and progressive, but reversible, disturbance of the uptake of radioactive iodine ( $I^{131}$ ) by the thyroid gland was found in rats subjected to tourniquet shock. The conversion to organic-bound iodine was apparently not affected early in shock but was affected, again reversibly, late in shock. The authors believe the disturbance may represent either an increased or decreased thyroid activity. Adrenalectomy did not significantly alter the disturbance.

In two series of experiments whole thyroid glands from both control and shocked animals were incubated for thirty and one hundred and twenty minutes in a buffered  $I^{131}$  solution. These *in vitro* studies showed no demonstrable disturbance of uptake or organic conversion early in shock and only a slight change late in shock.

Four charts; 2 tables.

**Effect of Adrenalectomy and DCA on the Radioisotope Intramuscular Clearance and Distribution in the Rat.** Frederick R. Franke, Joseph B. Boatman, and R. S. George. *Angiology* **2**: 46-50, February 1951.

Radiosodium and radioiodine muscle clearance studies were carried out in a series of adrenalectomized rats, some of which were maintained on DCA (desoxycorticosterone acetate) and some on DCA and saline. The radiosodium clearance rate was decreased in the adrenalectomized animals and in the adrenalectomized animals maintained on DCA and saline; in the adrenalectomized group maintained on DCA alone, radiosodium clearance was increased.

Radiosodium clearances varied under experimental

conditions, while radioiodine clearances remained essentially the same; this indicates that the clearance of these radioisotopes may be dependent upon different factors and that the two cannot be used interchangeably to quantitate peripheral circulation.

The changes in the average concentration of radioiodine ( $I^{131}$ ) in the pituitary, thyroid, muscle, and liver of the animals under the experimental conditions of this study are recorded.

Two charts.

**Disappearance of Isotopically Labeled Gold Colloids from the Circulation of the Dog.** C. W. Sheppard, Gilbert Jordan, and P. F. Hahn. *Am. J. Physiol.* **164**: 345-350, Feb. 1, 1951.

Experiments carried out by the authors showed that immediately following injection of radioactively tagged colloidal gold particles in the dog the circulatory level drops exponentially with time, the half-value time being about one and a half minutes. A very low residual level is reached in about ten to twenty minutes, showing occasional fluctuations. A high concentration of activity is then found in the buffy coat fraction, and if blood is withdrawn and transfused into a second animal the initial rapid rate of decline is not observed.

The possibility is explored that the rate of the initial disappearance might be quantitatively related to the total blood flow rate to the liver.

Seven charts; 2 tables.

**Dynamic Aspects of Sodium Metabolism in Experimental Adrenal Insufficiency Using Radioactive Sodium.** Thomas N. Stern, Vinton V. Cole, Anne C. Bass, and R. R. Overman. *Am. J. Physiol.* **164**: 437-449, Feb. 1, 1951.

The work of Flanagan, Davis, and Overman (*Am. J. Physiol.* **160**: 89, 1950) showing a loss of extracellular sodium and chloride to some body tissue in acute adrenal insufficiency is confirmed. Analyses of liver, spleen, heart, muscle, brain, skin, and gut did not reveal increased sodium, but an elevated chloride concentration was found in muscle, heart, and brain. Bone, as represented by the mid-femur, was shown not to have a detectable increase in sodium concentration during adrenal insufficiency.

Radioactive sodium was employed to study sodium turnover in acute adrenal insufficiency. Erythrocyte sodium turnover was measured in 11 normal dogs and 5 bilaterally adrenalectomized dogs in insufficiency. Although the trend was toward a more rapid turnover rate in insufficiency, no statistically significant difference appeared in this small series. The relative activities of liver, muscle, heart, gut, and skin for dogs in adrenal insufficiency was not different from normal at the time intervals measured; however, if such differences exist, they may have been masked, since the tissues were sampled at times when they were near  $Na^{24}$  equilibrium with the extracellular fluid. The radioactivity data indicate that sodium metabolism in bone is drastically altered in adrenal insufficiency, since both the height and shape of the relative specific activity curve for bone in the adrenalectomized dog are obviously different from normal.

Three charts; 5 tables.

## RADIATION EFFECTS; PROTECTION

**The Histamine Hypothesis of the Biological Effects of Radiation.** F. Ellinger. Schweiz. med. Wchnschr. 81: 61-65, Jan. 20, 1951. (In German)

The author reviews here his earlier experimental work indicating a great similarity between the local and distant reactions after irradiation and the administration of histamine. Animals which were sensitive to histamine were sensitive also to radiation. Animal experiments have shown also that there is an increase in histamine or histamine-like substances in the skin and blood following irradiation. These substances are either freed by cell destruction or newly formed by a radiochemical reaction. It is believed that there are several of these substances and that the latent period of the radiation effect can be explained by the different sensitivity of the cells.

The conclusion is reached that the histamine hypothesis of radiation effects is experimentally and clinically well founded. It has been of value in the treatment of radiation sickness as a basis for the administration of antihistamine substances. [See papers by Ellinger in Radiology 44: 241, 1945; 51: 394, 1948].

EUGENE F. LUTTERBECK, M.D.  
Chicago, Ill.

**Late Radiation Reaction in the Small Intestine Manifest Eight Years After Therapy. Report of a Case.** Ralph C. Frank and Ernst A. Pohle. Ann. Surg. 133: 104-108, January 1951.

The authors describe the clinical course, radiologic, and pathologic findings in a patient in whom radiation injury of the small intestine was found eight years after therapy. The original lesion in this case was a carcinoma of the ascending colon. Two years after surgical removal of the carcinoma, a recurrence developed at the operative site. After re-exploration, and resection of a mass, roentgen therapy was given to 20 X 20-cm. abdominal ports anteriorly and posteriorly with a beam of 2.4 mm. Cu half-value layer. Three courses were given over a period of ten months, a total of 4,600 r being delivered to each port during this time.

Roentgen examination eight years after the therapy disclosed a dilated loop of ileum, and a diagnosis of small bowel obstruction was made. Resection of the involved segment was performed. Grossly, this measured 28 cm. and was folded into loops, which were matted together. The wall was thickened. Sections showed inflammatory edema with granulation tissue in the mucosa and submucosa. There was no evidence of neoplasm.

Five illustrations.

I. R. BERGER, M.D.  
University of Louisville

**Fibrosarcoma Developing in Heavily Irradiated Skin.** Calvin B. Stewart and William J. Pendergrast. J. M. A. Georgia 40: 24-25, January 1951.

The authors report a case of fibrosarcoma subsequent to irradiation of carcinoma of the lip. The initial lesion was treated in December 1929 with a radium mold for 250 mg. hours and with interstitial radium for 99 mg. hours. In August 1950, nearly twenty-one years later, the patient presented an elevated, crusted, indurated lesion 1.5 cm. in diameter in the radiation

scar of the lower lip. The diagnosis of fibrosarcoma was proved histologically.

The authors cite Wilson and Brunschwig (Surgery 2: 607, 1937. Abst. in Radiology 31: 125, 1938), who found that 19 of 25 cases of fibrosarcoma subsequent to irradiation developed in areas of chronic infection, either tuberculosis of bone or lupus of the skin. Six of the 25 cases followed therapy for cancer, hypertrichosis, or eczema.

Two photomicrographs.

I. R. BERGER, M.D.  
University of Louisville

**Repair of Large Radiation Ulcers Situated over the Heart and the Brain.** John Marquis Converse, Ross M. Campbell, and William L. Watson. Ann. Surg. 133: 95-103, January 1951.

Plastic repair of large skin and subcutaneous defects following radiation therapy may require skin and subcutaneous tissue from a distant source. Because of reduced vascularization of the proposed recipient site, the transplanted flap of skin must be provided with an autonomous blood supply.

In each of the 2 cases recorded here, the defect was extensive and situated over vital areas limiting further excision, the pericardium in one case and the dura in the second. The authors describe and show by line drawings the technic used in each case. They used a pedicled skin flap, which is a closed flap without raw areas open to infection. The flap was raised from the abdomen, attached to the forearm, and subsequently transferred to the defect.

Thirteen drawings; 6 photographs.

I. R. BERGER, M.D.  
University of Louisville

**Protection of Personnel Engaged in Roentgenology and Radiology. Final Report.** F. T. Hunter and L. L. Robbins. New England J. Med. 244: 9-13, Jan. 4, 1951.

This is a follow-up of a previous study by Hunter *et al.* reported in 1949 (New England J. Med. 241: 79, 1949. Abst. in Radiology 54: 925, 1950).

Film badge monitoring has produced several important results. Consciousness of a hazard because a badge is worn has made personnel more careful. Radiologists, residents, nurses, and technicians have learned greater respect for the tools with which they work. Technical improvements in design of a fluoroscopic table has already been utilized by some manufacturers. Architects have obtained better knowledge as a basis of new departmental designs.

Monitoring of radium-handling personnel showed that they were subjected to unusually hard radiation. This was ultimately traced to exposure which penetrated protective lead screening.

A statistical analysis of repeated blood count studies on 55 individuals showed no relationship of variations in the leukocyte count and in the polymuclear and eosinophil percentages to the average weekly exposure or the number of years the worker had been engaged in roentgenology. Individual deviations from the normal blood picture, which had caused anxiety in the past, are believed to be unrelated to x-ray exposure.

A suggestion is made that since monitoring is a



preventive measure, it is a proper function of public health departments.

Three graphs.

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**Protective Power of Roentgen Gloves.** Ragnar Steinert. *Acta radiol.* 35: 45-48, January 1951.

The leaded rubber used for gloves has, as a rule, a lead equivalent of 0.1 to 0.7 mm., i.e., lead rubber of 1 mm. thickness offers the same amount of protection as 0.1 to 0.7 mm. of lead.

The bare hand, during fluoroscopy at 70 kv., 3 to 4 ma., with standard equipment, receives about 4 to 8 milliroentgens per minute, a considerable dose. Measurements made with condenser chambers inserted in the glove fingers revealed an acceptable degree of exposure using leaded gloves of equivalent 0.28. Gloves having an equivalent of 0.5 afford, for practical purposes, perfect protection. Caution is advised against blind acceptance of manufacturers' statements of lead equivalent.

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## EXPERIMENTAL STUDIES

**Acute Intestinal Radiation Death. Studies on Roentgen Death in Mice.** III. Henry Quastler, Elizabeth F. Lanzl, Mildred E. Keller, and James W. Osborne. *Am. J. Physiol.* 164: 546-556, Feb. 1, 1951.

If mice are given whole body irradiation with 400 r, a small percentage will suffer acute death in about eleven and a half days. As the dose is increased, the number of fatalities rises, but the mean survival time of the animals which die during the acute period remains near eleven and a half days. As the percentage of deaths approaches 100, the mean survival time begins to decrease, and continues to do so, with increasing dose, until a value of three and a half days is reached. At this level, the survival time again remains stable, even if the dose is increased as much as tenfold. It is only after extremely high doses that this "acute" effect is superseded by the "hyperacute" reaction, with death occurring very rapidly. Thus, mice must have intrinsic properties which favor survival times of eleven and one-half and three and one-half days. These times are called *characteristic values of the response spectrum of the mouse*.

It was found that three and one-half days was a characteristic value of the response spectrum in mice of different strains and of almost all ages. Split-dose experiments showed that after an x-ray dose has been administered which kills in three and one-half days, additional irradiations do not further modify the life expectancy, and that a mouse can be made to die three and one-half days following irradiation with a smaller dose, if a large supplementary dose is administered after a suitable time interval. Experiments on partial body irradiation of mice revealed that the three and a half day process is elicited if, and only if, any large portion of the intestine is irradiated. Thus, it is not necessary to expose the whole body to radiation. The three and a half day process, therefore, is called "acute intestinal radiation death."

Some hypotheses concerning the mechanisms involved are discussed.

Three charts; 2 tables.

**Effect of Acute Whole-Body X-Irradiation Upon Water and Electrolyte Balance.** Robert J. Soberman, Richard P. Keating, and Roy D. Maxwell. *Am. J. Physiol.* 164: 450-456, Feb. 1, 1951.

Disturbances in water and electrolyte balance in acute radiation syndrome are suggested by a number of observations on human beings and animals exposed to large amounts of ionizing radiation. Vomiting and diarrhea were observed in many of the Japanese exposed to the ionizing atomic bomb radiation, and examination of necropsy material revealed edema of

many organs. Because of the inconclusive results of previous studies, the authors decided to reinvestigate the effects of acute whole-body x-irradiation on water and electrolyte balance. Simultaneous repeated measurements of total body water, extracellular space, sodium space, whole blood, red cell and plasma volume, and plasma electrolytes were carried out in adult female dogs following 450 to 500 r whole-body x-irradiation. Except for an increase in plasma volume and a decrease in red-cell volume, no consistent changes were noted in any of the determinations.

**Experimental Studies on Early Lens Changes After Roentgen Irradiation. I. Morphological and Cytochemical Changes.** Ludwig von Sallmann, with the technical assistance of Carmen M. Munoz. *Arch. Ophthalmol.* 45: 149-164, February 1951.

Fifty-nine chinchilla rabbits (71 eyes) were subjected to a single dose of 2,000 r of penetrating roentgen rays, with the following radiation factors: 220 kv., 20 ma., 145 r per minute in air, 0.5 mm. Cu plus 1 mm. Al filtration, 30 cm. target-skin distance, 20 mm. field (round); half-value layer, 1 mm. Cu. The anesthetized animals were fastened to a board so that one eye of each could be irradiated while the other, shielded, remained outside the beam. The upper lid of the eye to be irradiated was fastened open and the roentgen beam directed from above. In 53 rabbits the upper limbus was centered in the field and the margin of the lids kept within the field; in 6 rabbits the beam was aligned with the optical axis. In an additional series of 17 rabbits (23 eyes) a dose of 1,000 r was used twice, the second being given either one week or three weeks after the first. Repeated observations with focal illumination, with the biomicroscope, and with the ophthalmoscope were made at intervals ranging from twenty-four hours to two weeks over periods varying in length up to one year.

Cataractous changes became demonstrable with the ophthalmoscope in 53 of 56 eyes observed longer than a month within four to ten weeks after irradiation with 2,000 r. The opacities started at the equator of the lens and progressed in the posterior cortex, and then in the anterior cortex, in characteristic patterns.

Acute exposure to a dose of 2,000 r was followed histologically as early as one week after irradiation by spatial disarrangement and initial morphological changes of the nuclei in the bow and in the pre-equatorial zone of the lens epithelium. In the second and third weeks degenerative changes of the nuclei in this area became more pronounced, with a considerable decrease in the number of these tissue elements and with gaps in the epithelial row of the pre-equatorial zone.

Swelling and disorganization of lens fibers were usually observed after changes in the cell nuclei had advanced, but in 6 of the 56 irradiated eyes of the series extensive cystic formations at the subcapsular ends of the lens fibers four weeks after irradiation suggested a direct radiation effect on the cytoplasm.

The content of desoxyribonucleic acid in nuclei of normal lens epithelium could be well demonstrated by the Feulgen technic, and the highly polymerized form of the acid could be shown with methyl green. The nuclei of the germinative zone appeared especially rich in this constituent. Staining for ribonucleic acid in the cytoplasm with pyronin did not give reliable results.

The cytochemical studies indicated that two weeks after irradiation individual nuclei in a given area contained less desoxyribonucleic acid of high polymerization than nuclei in a comparable area of the control lens, but it was not clear whether or not the staining differences preceded the structural signs of nuclear degeneration.

Five figures; 3 tables.

**Alterations in Thermal Fragility of Rat Erythrocytes Following Total Body X-Irradiation.** Leontine Goldschmidt, Robert L. Rosenthal, Victor P. Bond, and Maurice C. Fishler. *Am. J. Physiol.* 164: 202-206, January 1951.

Three factors, namely, bone marrow inhibition, hemorrhage, and direct destruction of red cells, appear to contribute to the anemia following exposure to ionizing radiation. A review of the literature reveals indirect but not direct evidence that radiation causes red cell destruction. A method has been developed by the authors by which definite changes in red cell integrity can be demonstrated within twelve hours after exposure of rats to total body x-irradiation. With this technic the amount of hemolysis produced by exposure of red cells to an elevated temperature (53° C.) is measured quantitatively by spectrophotometric means. The method is based upon the previous demonstration that the extent of hemolysis is quantitatively related to duration of exposure and degree of temperature elevation to which red cells are exposed. A definite increase in red cell fragility was found four to twelve hours after exposure of the animals to total body roentgen irradiation with 500 and 600 r.

**Hyaluronidase Action in Normal and in Roentgen-Irradiated Rabbit Skin.** Ray O. Noojin and Hugh B. Praytor. *Arch. Dermat. & Syph.* 63: 191-198, February 1951.

Hyaluronidase is an enzyme possessing the ability to dissolve the cementing substance between tissue cells. In order to determine if x-ray therapy produced any change in hyaluronidase activity, the following experiment was done:

Three groups of rabbits had a single irradiation of the left side of the trunk with x-rays generated at 85 kv., with a half-value layer of 0.7 mm. Al. One group received 400 r, another 800 r, and another group 1,600 r. An additional group received no irradiation. One week later all the animals were given two small injections of India ink into the skin of each flank, one injection containing a quantity of hyaluronidase and the other a small amount of sodium chloride. Readings to determine the spread of the ink were made at

various intervals in the first hour and also at twenty-four and forty-eight hours thereafter. The injections and readings were repeated five weeks later, except in the group of rabbits which had received 1,600 r. These were re-injected earlier than the others, since 50 per cent had already died by the third week following irradiation. When comparisons were made within each group between the spread of India ink with hyaluronidase in the treated and in the untreated flank, either one week after irradiation or later, the results obtained were not significantly different. The same observation was true in the rabbits receiving x-ray therapy sufficient to kill half of the group and also true of readings made on the spread of India ink and sodium chloride.

It appears that within the first few weeks after the administration of roentgen therapy to rabbits, the spreading effect of hyaluronidase in the skin is not significantly altered.

Eight figures; 3 tables.

CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Experimental Arterial Stenosis: Post Stenotic Dilatation and Collateral Blood Flow.** J. Flasher, D. R. Drury, and G. Jacobson. *Angiology* 2: 60-70, February 1951.

Arterial stenosis may be associated with an increase in the size of the post-stenotic portion of the artery, as well as with an increase in the size—and possibly the number—of the collateral vessels. In the present study the authors were primarily interested in the degree and extent of the post-stenotic dilatation, and the role of tissue ischemia in producing it.

A constricting tie or clip was applied to the left renal artery in 16 rabbits, and the right kidney was either not manipulated at all or it was removed. The renal circulation was then investigated angiographically and by surgical exploration with direct visualization. Dilatation of part or all of the post-stenotic portion of the artery occurred in 12 of the rabbits; in 4 it appeared to extend into the primary branches. The degree and extent of the dilatation appeared to be related to the degree of renal tissue ischemia, i.e., to the degree of hypertension. In the 4 rabbits in which a post-stenotic dilatation failed to develop, hypertension did not occur. It is thought that the renal artery constriction was insufficient to produce any or sufficient renal ischemia in these animals.

There was no apparent collateral blood flow in relation to the renal artery in the normal rabbit, under the conditions of the experiments. Six of the 12 rabbits that exhibited the post-stenotic dilatation were investigated for and all showed evidence of a collateral circulation. Two of the 4 rabbits in which post-stenotic dilatation failed to develop exhibited no evidence of a collateral circulation. Therefore, the initiation of a collateral blood flow appears to be related to the presence of renal ischemia. If this flow merely represents the opening up of previously present but non-functioning vessels, then the alteration of pressure gradients, occasioned by the constriction of the renal artery, might also be an adequate explanation.

The authors' experiments do not indicate whether the above changes are due to a substance produced in the ischemic renal tissue or to defective excretion or absorption of a substance by the ischemic or curtailed renal tissue. The former appears to be more likely.

Twelve angiograms; 1 table.

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